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VOLUME 1 NUMBER 2

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Vol. I FEBRUARY, 1919 No. 2

A CASE OF OCCLUSION OF THE POSTERIOR INFERIOR CEREBELLAR ARTERY WITH CARDIAC MANIFESTATIONS AND INVOLVEMENT OF THE LEFT VAGUS NUCLEUS *

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NEW YORK

The typical syndrome which this case presents and the unusual cardiac complications which it manifests, have an important bearing on certain physiologic problems with regard to the course of the sensory tracts in the medulla, and the influence of the vagus on the heart action.

REPORT OF CASE

History.—L. A., a man, aged 48, born in Austria, was admitted to the Neurologic service of the Mount Sinai Hospital, May 29, 1918, complaining of persistent hiccough.

His present illness began gradually five days before admission (Friday). He had felt perfectly well that day until the evening, when he experienced the sensation of nausea and fatigue immediately after finishing a heavy meal. He sought relief by going to bed. The next morning (Saturday), despite a good night's rest, this feeling of nausea persisted. In addition he developed subjective dizziness, which was aggravated by sitting and walking. His gait became unsteady, and he occasionally staggered as if drunk. He experienced marked fatigue. He suffered no headaches, nor at any time did he have any loss of consciousness. The following morning (Sunday), while being shaved at the barber's, he was suddenly seized by a queer sensation; he felt as if his body were being cut in half by a sharp knife. He immediately returned home without assistance and took to bed. That afternoon he began to hiccough, and this has since been the most persistent and annoying symptom of the disease. The next day (Monday), he became very weak and had to be helped about. His voice suddenly became hoarse and rasping in quality. His hiccough ceased spontaneously for about half an hour. He began to complain of coldness in both legs, and a dull nonradiating pain in the right arm. He had no visual auditory, olfactory or gustatory disturbances; no vesical or rectal disturbances, no dysphagia or vomiting.

His past history presents the usual diseases of childhood; typhoid twenty years ago and asthma for the past fifteen years. He is a man of temperate habits, smoking but little and taking alcohol in moderation. He denied venereal disease by name and symptom. He was a furrier twenty years ago, in which

* From the Neurological Service of the Mount Sinai Hospital, New York.

occupation he was engaged for five years. He has since led an easy and quiet life.

About four years ago he experienced right lumbar pain, with difficulty in micturition, but without hematuria. The diagnosis of nephrolithiasis or nephritis was made by a physician. Until one year ago he had no frequency of urination; since then, however, he has been compelled to void six times a day and once at night. He has had no pruritis, polydipsia or polyphagia. Urinalysis in 1913 was reported negative.

The earliest premonitory symptoms of his present illness made their first appearance six months ago, when he began to develop a dull nonradiating pain in his right arm, and became subject to attacks of dizziness and staggering. These attacks were at no time associated with loss of consciousness. At first they visited him but once a fortnight, and were very short in duration, lasting usually no more than a few minutes. Just before the onset of his present condition, they became more frequent, occurring twice in one week.

His family history, otherwise irrelevant, reveals the fact that his sister has had diabetes for many years.

Physical Examination.—The patient is an obese, gray-haired, middle aged man who is incessantly hiccoughing. His general condition is fair; he is uncomfortable, and hesitates to sit up on account of fear of producing an attack of vertigo. He is intelligent; his attention is good, but his memory is very poor. His voice is hoarse and rasping in quality.

The face shows a slight weakness of the left side. The left palpebral fissure is narrower than the right. There is a subacute conjunctivitis present in his left eye. The corneal reflex was found to be absent on that side and sluggish on the right. The pupils are unequal; the left is smaller than the right and also irregular in outline. They both react briskly to light and accommodation. All ocular movements are normal in range. In the extreme position there is a slight horizontal nystagmus, especially on looking to the right. All movements of the jaw are normal. The teeth and gums reveal a marked pyorrhea alveolaris. The tongue protrudes in mid line and presents a fine fibrillary tremor; there is no atrophy. The palate moves freely. The uvula is in midline. The left vocal cord is paralyzed (left recurrent palsy). There is no difficulty in swallowing. The pharyngeal reflex is absent on both sides.

Special Senses.—Smell, taste, and hearing are unaffected. Visual fields and fundi are normal. The vertical and horizontal semicircular canals were tested by the Bárány method. The ears were douched with cold water of a temperature of 68 F. The following results were obtained:

Stimulation of the left vertical canal produced a marked horizontal nystagmus to the right after forty-five seconds. It did not cause him any vertigo, pass-pointing or nausea.

Stimulation of the left horizontal canal produced a marked horizontal nystagmus to the right. The patient complained of vertigo, but no nausea. The right arm pass-pointed to the left by three inches. The left arm did not pass-point.

Stimulation of the right vertical canal produced a horizontal nystagmus to the left after fifty seconds, which was more marked in the left eye. There was no vertigo or nausea. The right arm pass-pointed 4 inches to the right, whereas there was no pass-pointing with the left arm. Stimulation of the right horizontal canal produced a marked horizontal nystagmus equal to both eyes. The patient experienced slight vertigo, but no nausea. The right arm pass-pointed 1 inch to the right, and the left arm 5 inches to the right.

These tests were done on August 3, and repeated for confirmation nine days later. At both sittings practically the same results were noted.

Motor System.—The movements of the head and trunk are unrestricted. Although the musculature of all the limbs is flabby, there is no atrophy. The motor power on extension and flexion is much weaker in the left upper extremity than in the right. The grasp in the left hand is very much diminished. On attempting to carry out rapid successive movements of pronation and supination, adiadokokinesia is manifested in the left hand. There is also some degree of ataxia in that hand, with by-pointing to the left. There is no asterognosis or tremor. The left lower extremity shows a similar degree of ataxia and motor weakness, as compared with the right. There is no restriction in the range of movement of any of the extremities. His gait cannot be tested on account of generalized weakness and marked discomfort.

Reflexes.—The abdominal and cremasteric reflexes are sluggish, the right more so than the left. The left plantar reflex gives a normal flexor response, whereas the right exhibits a tendency to a Babinski and manifests a Chaddock which is suspicious, but not definite. The Gordon, Mendel-Bechterew, Strümpell and Oppenheim reflexes cannot be elicited.

The tendon reflexes in the upper limbs are sluggish, the right more so than the left. The patellar tendon reflexes are sluggish but equal. The ankle jerk is absent on both sides. There is no ankle clonus.

Sensations.—Spontaneous sensations: He complains of a dull non-radiating pain in the right arm. (There are no arthritic changes). The right side feels cold and numb as if dead. These sensations are constant and not aggravated by external agents.

Touch: Light touch, as measured by cotton-wool and von Frey's hairs, and pressure touch, as tested by the pressure esthesiometer, are both perfectly preserved over the face and body.

Localization is perfect on both sides. Roughness is recognized equally well on both sides.

Tickling and scraping: These stimuli, which were used by reason of their affective component, were found to be normal.

Vibration: The threshold for vibratory sense, although diminished, is equal on both sides.

Compasses: He was unable to discriminate two points either when applied simultaneously or in rapid succession on both sides.

Pain: Superficial pain as tested by the pressure esthesiometer and algesimeter, is lost on the right side of the body and left side of the face.

Pressure pain, as measured by Cattell's algometer, although not lost, is very much diminished on the right side of the body and left side of the face. (Refer to Figs. 1 and 2).

Cardiac Manifestations.—Associated with this neurologic status is the unusual cardiac phase of the disease. The heart is normal in size, shape and position. The rate is slow; the average being 68 per minute. The sounds are of fair quality, and are heard over long periods as a normal rhythmic series, which is occasionally interrupted by extra-systoles, especially after a spell of hiccoughing. There are no murmurs. The radial pulses are small and equal, and correspond to the heart's action. There is no pulse deficit.

Clinical Findings.—The systolic blood pressure is 120 mm. of mercury; diastolic pressure is 90 mm. The total and differential leukocyte counts are normal. The blood and cerebrospinal fluid Wassermann tests are negative.

The spinal fluid is clear, under normal pressure and contains seven cells per cm. The urine contains from 2 to 4 per cent. sugar on an ordinary soft diet. The blood sugar is 0.332 per cent. by the Epstein method. The urea nitrogen and the incoagulable nitrogen of the blood and the carbon dioxid tension are normal.

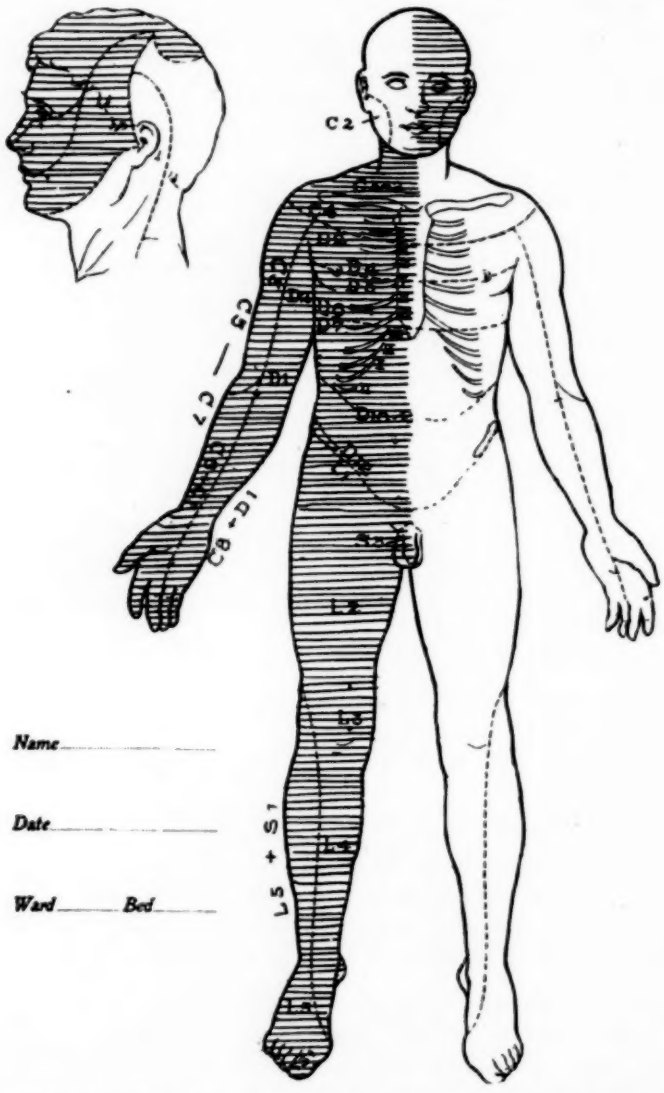

Fig. 1.—Anterior view; sensory disturbances. Shaded areas represent analgesia and thermanesthesia.

Progress of the Disease.—The most annoying symptom has been the almost incessant singultus, which was best controlled by large doses of chloral by rectum. This was the only measure which afforded sleep and relief. On June 8, nine days after admission, the singultus became less marked, and on June 12,

it ceased completely. It has returned at rare intervals, but only for very brief periods and disappeared spontaneously. Temperature: Both epicritic and protopathic thermal sensibilities are lost over the same areas. (Refer to Figs. 1 and 2).

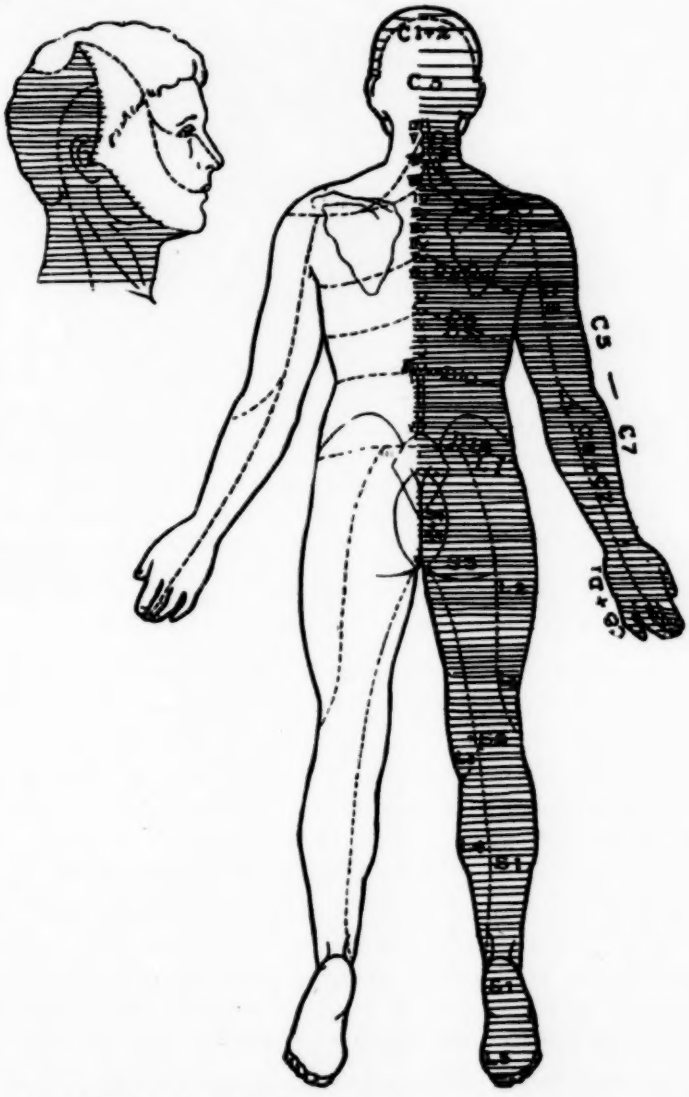

Fig. 2.—Posterior view. Sensory disturbances. Shaded areas represent analgesia and thermanesthesia.

Position: The power of recognizing the posture of any part of the body is unimpaired.

Passive and active movements are normally appreciated.

Weight appreciation is unaltered.

The appreciation of size, shape, form, texture and consistence is normal.

SUMMARY

Face.—Both halves of the face respond equally well to cotton wool and von Frey's hairs, but over the left forehead, temple and cheek, the appreciation of heat, cold, and superficial pain is lost; pressure pain is very much diminished, but not lost. The threshold for vibratory sense, though equal, is lowered on both sides. Two-point recognition is lost.

Body.—All forms of tactile sensibility are perfectly preserved, vibration is appreciated, but diminished, and localization is perfect on both sides. Weight, size, shape and form are accurately recognized. The compass test is impaired on both sides. Over the entire right side superficial pain is lost; the pressure necessary to cause pain is uniformly higher than over similar parts on the opposite side. Over the same area on the right half of the body he is insensitive to all degrees of temperature, and the borders of this loss of sensation correspond to those of the analgesia. Passive and active movement and posture recognition are normal.

The neurologic status has undergone but few changes. The left facial weakness has become more pronounced. On June 15, flattening of left forehead and contracture of the left face became evident. On June 28, wasting on that side was noticed in the region of the masseter muscle, while the jaw was slightly pulled over to the right. The sensory and other changes have remained the same. The cardiac cycle is described in the latter part of the paper.

As the general condition improved, a rigid diabetic regimen was established, and Allen's treatment instituted. He very quickly became sugar-free and has remained so despite a very liberal diet, rich in fats, proteins, and carbohydrate.

GENERAL CONSIDERATIONS

Anatomy.—The posterior inferior cerebellar artery is the largest branch of the vertebral artery. It arises a short distance below the pons and passes obliquely backward around the medulla, at first between the roots of the hypoglossal nerve and then between the roots of the spinal accessory and vagus nerves (Cunningham) toward the vallecula of the cerebellum. As it winds around the medulla, it gives off small terminal arteries to the ventral and lateral aspect, and this region therefore is especially liable to necrosis when the main vessel is blocked. The region affected extends from the point where the inferior cerebellar peduncle begins to pass into the cerebellum, to the middle of the hypoglossal nucleus below. The structures most involved are the greater part of the formatic reticularis and its nuclei; the descending root of the fifth and cells in association; the nucleus ambiguous and glossopharyngeal nucleus and their nerves; the ventral and dorsal spinocerebellar tracts, and other tracts (Olivo-cerebellar), passing into the inferior cerebellar peduncle. The mesial fillet is supplied by twigs from the anterior spinal artery and escapes.[1] The area described is outlined in Figures 3 and 5.

1. Ferrier, David: Albutt and Rolleston System, 1910, **8.**

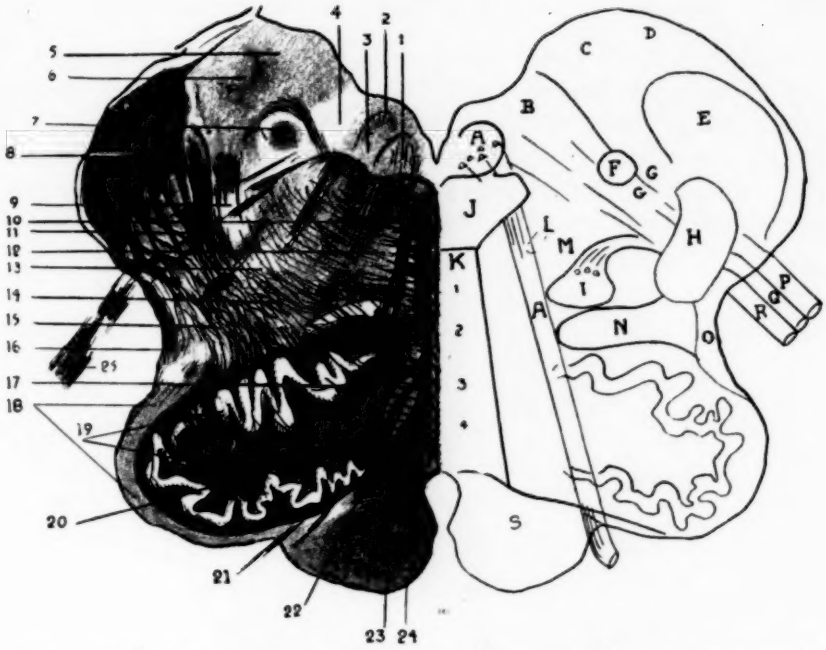

Fig. 3.—Modelled after drawings by Villiger and Edinger. The section passes through the level of the inferior olive. The shaded half presents the histologic anatomy of the region, whereas the schematic half represents the results of lesions in the corresponding parts.

Shaded Area: 1, Nucleus N. XIII; 2, Fasciculus longitudinalis dorsalis (Schütz); 3, nucleus intercalatus Staderini; 4, nucleus alae cinerae s. N. X dorsalis; 5, nucleus vestibularis medialis Schwalbe; 6, nucleus vestibularis lateralis (Deiters); 7, Tractus solitarius and nucleus tractus solitarii; 8, Corpus restiforme; 9, nucleus radicis spinalis trigemini; 10, fasciculus longitudinalis medialis; 11, radix spinalis trigemini; 12, substantia reticularis grisea; 13, nucleus ambiguus; 14, fibri olivo-cerebellaris; 15, nucleus lateralis; 16, tractus Gowers; 17, lemniscus medialis; 18, tractus thalamo-olivaris; 19, oliva inferior; 20, hilus olivae; 21, nucleus hypoglossus; 22, nucleus olivar. accessor. medialis; 23, pyramis; 24, fibrae arcuatae externae ventrales.

Within the substantia reticularis, dorsal to the olive and lateral to the fillet, numerous longitudinal crossing fibers are seen; these may be considered as association fibers, that serve to unite different segments of the medulla oblongata with one another, with higher lying parts of the brain and the spinal cord. Ediger has pointed out that probably within this formatio reticularis run those connecting fibers which associate the facial, vagal and phrenic nuclei to coordinated activity in respiration.

Schematic Half: *A*, atrophy and paralysis of the tongue; *B*, slowing of pulse and respiration; *C*, nystagmus and falling toward side of lesion; *D*, anesthesia of skin and loss of deep sensibility on side of lesion (which in this section is lower than on corresponding side); *E*, asynergy on side of lesion; *F*, ageusia; *G*, vasomotor disturbance, perspiration, psosis, myosis; *H*, anesthesia of skin and mucous membranes of head, loss of corneal, etc., reflexes; I, aphonia, difficulty in swallowing; J, impairment of nodding of head and of blinking; *K*, crossed muscle and skin (?) anesthesia, (1) sacrum, (2) legs, (3) trunk, (4) arms; *L*, partial crossed head anesthesia; *M*, loss of tonus and tendon reflexes; *N*, crossed analgesia and thermo-anesthesia of arms and legs; *O*, asynergy; *P*, anesthesia of larynx, etc.; *Q*, aphonia; *R*, cardiorespiratory disturbance; *S*, completely crossed spastic paralysis.

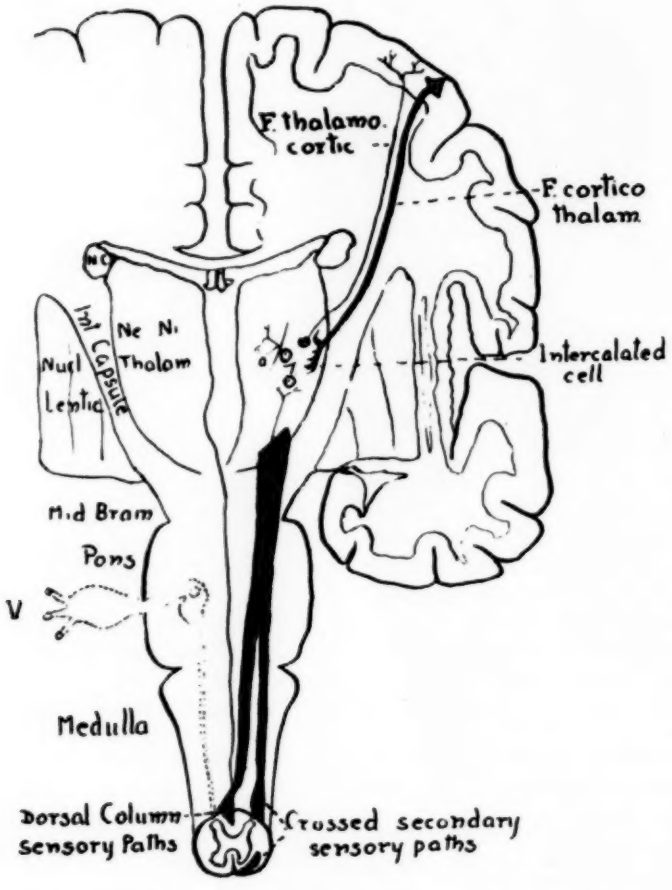

Fig. 4.—(After Head and Holmes.) Represents diagrammatically the anatomic arrangement of the paths and centers concerned in sensation. Two distinct paths exist in the spinal cord; a crossed secondary path in the ventrolateral column which conveys impressions of pain, temperature and touch, and a second uncrossed path in the dorsal columns, which also carries touch and in which run impulses that underlie the sense of position, appreciation of movement, and discrimination of two points and the recognition of vibration, size, shape, form, weight and consistence. This second path decussates in the lower part of the medulla oblongata, but separate from the first path, at least as high as the pons. All these secondary sensory fibers now crossed, terminate in the ventrolateral region of the optic thalamus. The impressions they carry are regrouped here and through neurons are distributed along two distinct paths; the one carries impressions to the cerebral cortex; the other we assume toward the more mesial parts of the optic thalamus. The corticothalamic fibers, which terminate in the lateral nucleus of the optic thalamus, are shown.

Sensation. — The brilliant studies of Henry Head and Gordon Holmes[2] have resulted in a clearer conception of the sensory disturbances from cerebral lesions. The impulses underlying the sensations of pain, heat and cold seem alone to run unaltered, though not uninterrupted, between the upper end of the spinal cord and the optic thalamus. These paths run up in the neighborhood of the nucleus

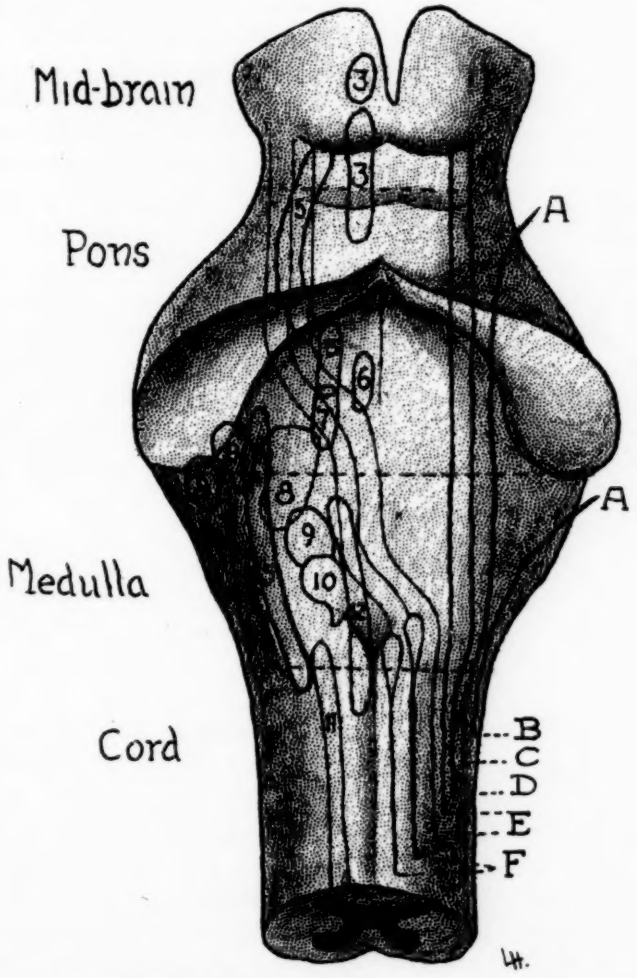

Fig. 5.—(After Dana.) Showing how lesions in the pons and medulla may cause focal symptoms by cutting off tracts and destroying cranial nerve nuclei. The motor tracts lie deep below the sensory and begin to cross in the lower medulla and cord. They are not indicated here. *A*, to cerebellum; *B*, direct cerebellar tract; *C*, spinocerebellar (Gower's tract); *D*, temperature and pain tract; *E*, tactile; *F*, muscle sense.

2. Holmes and Head: Brain, Lond. **34**: 1911.

of the trigeminal nerve (Fig. 4). This close association is particularly well shown by cases of occlusion of the posterior inferior cerebellar artery (Wallenberg, Breuer, Marburg and Spiller), as in this instance, where the sensory nucleus of the fifth nerve and spinothalamic tract in that region are involved. The peculiar, yet typical dissociation of sensation which this case presents is more readily understood on further analysis. The fibers for pain, temperature and touch are carried in the spinothalamic tract, which crosses to the opposite side about two or three segments above their point of entrance in the cord. The dorsal columns, which do not cross in the cord, carry the fibers for touch (in part), position, appreciation of movement, two point discrimination, vibration, size, shape, form, weight and consistence. These impulses travel together in the same columns of the spinal cord, but as soon as they reach the first synaptic junction, those impulses underlying the appreciation of posture and passive movement become separated from those concerned with spatial discrimination. (Compass test, size, shape, etc.[3]) This change evidently takes place at the posterior column nuclei. Before we can determine the exact paths that these finer differentiations would lead us to believe exist, a more elaborate anatomic and physiologic insight must be evolved by future study. Suffice it to say that we know that these subtle variations in the sensory mechanism do exist.

Bárány Tests.—After a careful study of the data obtained, it is difficult to reach a definite conclusion with regard to the significance of the above tests, even in the light of the recent contributions by Randall, Jones and Mills.[4, 5] Mills and Jones have attempted to demonstrate neuraxial differentiation of the fibers from the horizontal and vertical canals. In one of their cases,[4] in which the lesion was clearly thrombosis of the right posterior inferior cerebellar artery, the right horizontal canal failed to respond normally, whereas reactions from the right vertical canal were normal. Randall and Jones,[5] after an examination of 129 pathologic cases reached certain definite conclusions: that on each side the fibers from the horizontal canals go to the Deiter's group, thence to the cerebellum by way of the inferior cerebellar peduncle through to the cerebellar nuclei globosus, fastigii, and emboliformis, and then to the cortex of both sides; that the fibers of the vertical canals apparently have an entirely different course, going directly to the posterior longitudinal bundle, probably entering the cerebellum through its middle peduncle; that another group of

3. Holmes and Head: Brain, Lond. **34**:124, 1911.
4. Mills, C. K., and Jones, I. H.: J. A. M. A. **67**:1298, 1916.
5. Randall, B. A., and Jones, I. H.: Am. J. M. Sc. **151**:515.

fibers undoubtedly goes to the spinal cord; that the impulses which are concerned with vertigo pass through the cerebellum.

Up to the present time there has been no confirmation of this work.

Motor Manifestations.—The motor symptoms cannot readily be grouped with the rest of the clinical picture under a single anatomic lesion. The homolateral hemitaxia being of cerebellar type, can be attributed to unilateral affection of either the spinocerebellar tracts or restiform body; but the paresis of the left face, and left arm and leg can hardly be explained on the same basis. The fact that the paresis is unilateral would point to a contralateral lesion in the cerebrum or cerebral peduncle or frontal portion of the pons in consequence of the proximity to each other of the central facial neurons and pyramidal tract in these areas. The possibility of an intracranial neoplasm must be entertained, but the absence of the more important general symptoms of cerebral neoplasm—headache, vomiting, optic neuritis and atrophy with amblyopia resulting therefrom, increased intracranial pressure, etc., mitigates against this likelihood. Inasmuch as lesions of the medulla are often diffuse and disseminated, and are especially diverse in their symptomatology, owing to the complex relations of the medulla itself, it seems most logical to seek an explanation in the form of multiple thrombi involving more than one branch of the vertebrals.

Diabetes.—The question here arises whether the diabetes is a result of the central lesion or the cause of its inception. In this respect the patient's previous history, though not very definite, associated with a family glycosuria, leads one to believe that the diabetic element is probably a priori rather than a posteriori in the sequence of the disease, and may be viewed together with sclerotic changes in the vessels as the etiologic factor in producing the thrombosis of the posterior inferior cerebellar artery.

Cardiac Phase.—Probably the most striking phase of this case is the cycle of cardiac developments that the patient manifested under observation.

On admission, bradycardia, with a rate of 68 at the apex, and a corresponding radial pulse, was present. The regularity of the rhythm was occasionally broken by extra-systoles. The next day, May 30, a telecardiogram (Fig. 6) was taken, and it showed a bradycardia with a rate of 64 and left ventricular preponderance. The P-waves were abnormally high in all three leads. The T-waves were very tall in Leads I and II, semi-inverted in Lead III. One auricular extra-systole was recorded in Lead II.

Five days later, June 5, another telecardiogram was taken, and showed the previous left ventricular preponderance plus an auricular

flutter. The auricular was 300, whereas the ventricular response was arrhythmic and varied in paroxysms between 84 and 140 (Fig. 7).

To determine whether the auricular flutter still persisted, another telecardiogram was taken two days later, June 7. The auricular rate was found to be increased to 375, but an added phenomenon was now being manifested. There were numerous cycles showing auricular fibrillation, which the electrocardiographic laboratory looked on as probably a transitory stage. The following morning, June 8, the cardiac picture was more definitely defined clinically; there was a

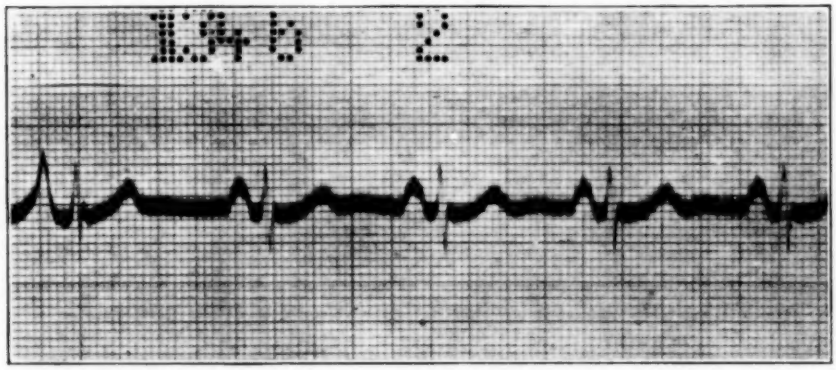

Fig. 6.—May 30, 1918, Lead II

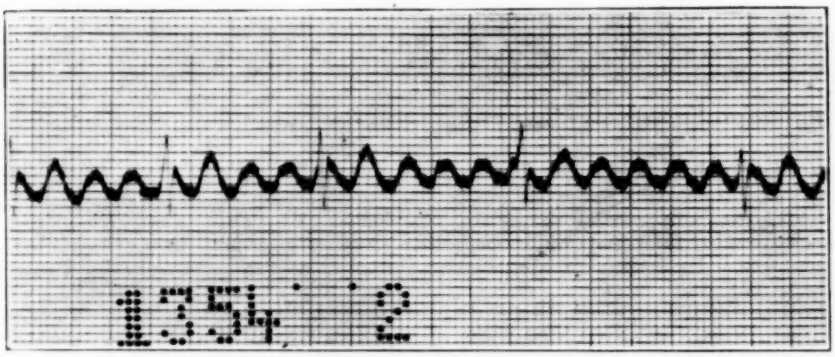

Fig. 7.—June 5, 1918, Lead II.

pulse deficit of 15, the apex beat was 108 and the radial pulse 93. The probable diagnosis of auricular flutter in the fibrillating stage was made.

On June 11, the heart was distinctly fibrillating; the pulse deficit was 10. This was confirmed four days later by a telecardiogram, which showed auricular fibrillation, and left ventricular preponderance and low voltage (Fig. 8). Under the influence of digitalis the

heart rapidly returned to normal rate and rhythm, and on June 22 the telecardiogram gave no evidence of auricular fibrillation or flutter. Several extra-systoles were recorded (Fig. 9).

These varied cardiac phases during the course of the disease present a rare opportunity to view the clinical picture from a physiologic standpoint. As well as could be determined by a careful history, the patient gave no evidence of previous cardiac disease. From the neurologic data we know that we are dealing with a lesion in the upper part of the medulla or lower part of the pons, in which the

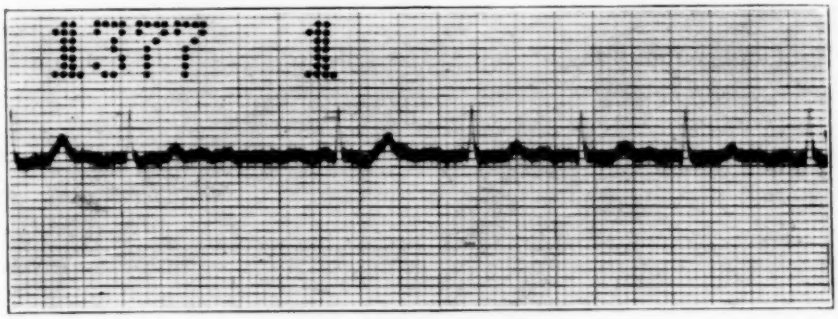

Fig. 8.—June 15, 1918, Lead I.

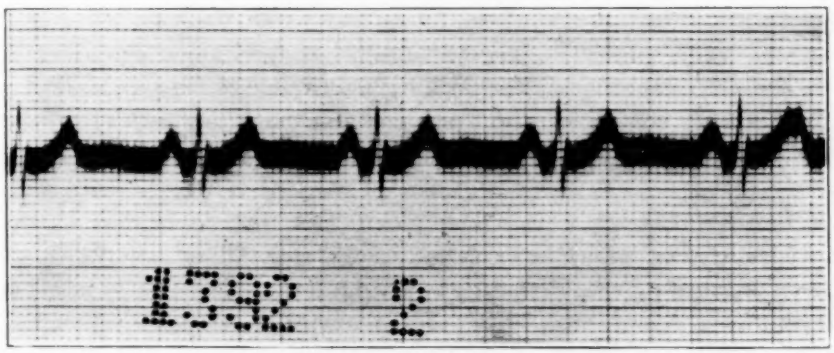

Fig. 9.—June 22, 1918, Lead II.

nucleus of the left vagus is involved. This would tend to confirm the studies that were made on the activities of the extra-cardial nerves and which have revealed marked functional differences in the right and left vagi and in the two cervical sympathetics. These differences are qualitative as well as quantitative.[6] Thus in his experimental work on dogs, Cohen,[7] found that stimulation of the right vagus usually caused arrest of all chambers of the heart, but appeared to have very

6. Hart: Abnormal Myocardial Function, 200.
7. Cohen: J. Exper. M. **16**:732, 1912.

slight direct influence either on conduction or on the activities of the ventricle. On the other hand, stimulation of the left vagus had only a moderate slowing effect on the auricles, but a very definite depressing influence on the rate of conduction between auricles and ventricles. His conclusions as to the differences in the distribution of the right and left vagus are shown in Figure 1. Robinson and Draper,[8] in their studies on conduction disturbances following vagus stimulation, reached the conclusion that the left vagus has as a rule a greater influence on the property of conduction than the right vagus.

The bradycardia, which was the first cardiac manifestation, may have been due to heightened vagus tone as a result of irritation of the pneumogastric center. But the phenomenon of auricular flutter is much more difficult of interpretation. Extensive observations have shown that it rarely occurs without some other damage to the cardiac tissue. It has been suggested by some that an abnormal balance of external nervous control may be an element in the production of auricular flutter, but no anatomic lesion which would indicate a removal influence or a hypertonic activity of the accelerators has thus far been demonstrated. The evidence in our case may lead us to suspect such a condition, though we have no indubitable ground to offer for its support. The event of fibrillation presents the same problem. It has been demonstrated that while the auricles are in flutter, vagus stimulation may change the flutter into a condition of fibrillation.[9] Morat and Petzetakis have been able to produce auricular fibrillation by stimulating the vagus and accelerator nerves. However, every heart showing fibrillation of the auricles which has been exhaustively examined, has given evidence of gross or histologic damage to its tissues, although it is a recognized fact that fibrillation of the auricles may be only temporary, as in our case. This would suggest that the cause may be of toxic or neurogenic origin. The problem is furthermore complicated by the almost immediate response which the administration of digitalis was able to call forth in our case. Pharmacologic studies have shown that digitalis acts in a two-fold manner on the functional activities of the heart. It has a direct effect on the muscle cells, and indirect influence through the vagus nerves.[10] It increases the tone and irritability of the heart muscle and stimulates the vagus. If we are to presume that the various cardiac manifestations in our case are due to vagus stimulation, it is hardly likely that the digitalis produced the return to normal by its central action, for

8. Robinson and Draper: J. Exper. M. **15:** No. 1, 1912.
9. Hart: Abnormal Myocardial Function, p. 118.
10. Hatcher and Wilbert: Pharmacology of Useful Drugs, 1915, p. 215.

further stimulation of the pneumogastric center would have tended to aggravate the condition.

Since by the administration of atropin, vagus impulses may be cut off and thus a clinical estimate be made of the influence which it has hitherto been exerting, $\frac{1}{100}$ grain of atropin three times a day was given hypodermically over a period of nine days. It had no effect whatsoever on the heart action in force, rate or rhythm.

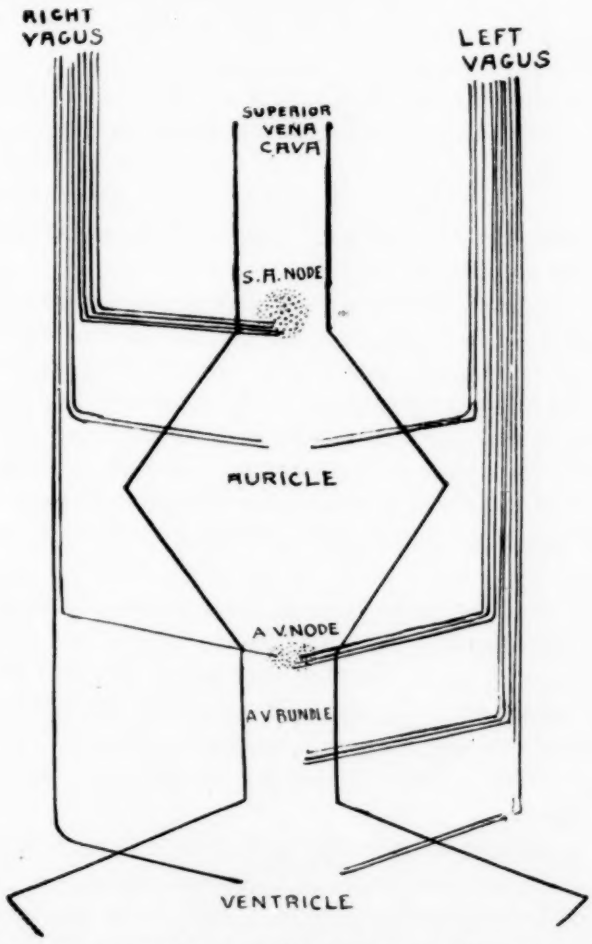

Fig. 10.—Diagram after Cohen modified by Hart indicating the distribution of the fibers of the right and left vagi and the right and left sympathetic. It is to be noted that the right vagus and the right sympathetic are, in the main, distributed to the sino-auricular node and the auricle. The left vagus and the left sympathetic have a preponderatiing influence over the auriculoventricular node and bundle. The data on which this diagram is based were obtained principally from the conclusions drawn from their experimental work, by Cohen, Rothberger and Winterberg.

It needs no further elaboration to indicate that the cardiac aspect of the case in the light of its neurologic background presents innumerable avenues of approach and interpretation, and tends to corroborate the physiologic experiments which have been conducted in many laboratories to explain the origin of the cardiac impulse.

SUMMARY

1. The case is one of occlusion of the left posterior inferior cerebellar artery with cardiac manifestations in a man of 48. The onset was gradual without loss of consciousness, but with a sense of giddiness, faintness and nausea, and a tendency to stagger occasionally to either side. This was followed a few days later by persistent hiccough and hoarseness.

2. In view of the presence of glycosuria and a family history pointing in the same direction, diabetes, together with arteriosclerosis, was considered the etiologic factor.

3. The symptoms resulting from this lesion embraced unilateral paralysis of the left vocal cord and the left side of the face, with anesthesia of the pharynx and absent corneal reflex in the left eye; myosis of the left pupil and narrowing of the left palpebral fissure; peculiar response to the Bárány test; and hemiataxy on the same side with alternate anesthesia of the left face and right side of the body. The sensory affection was of the dissociated type, pain and temperature sense being impaired, while tactile sensibility and muscular sense were intact.

4. In addition, the patient presented an abnormal cardiac function, which afforded ample opportunity for study with the electrocardiograph. Various irregularities were manifested; bradycardia, auricular flutter, numerous extra-systoles and auricular fibrillation. Atropin administered over a long period was unable to influence the heart action in any way. With digitalis, however, a favorable reaction was immediately obtained.

5. The symptoms in this case, besides their value from a regional diagnostic point of view, have an important bearing on the relation of the vagus center to the cardiac cycle. It is this object which prompted a record of the case in detail.

ADDENDA.—The patient left the hospital on August 28, apparently in good health, but with no change in the physical findings.

I wish to express my indebtedness and gratitude to Dr. I. Strauss for his guidance and suggestions; and to Dr. B. Sachs for permission to publish the case.

1 East One Hundredth Street.

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THE EYE AND AVIATION

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Samuel Johnson (1759), in his "Rasselas, Prince of Abyssinia," sets forth very graphically the principles of flying. He says:

> He that can swim needs not despair to fly; to swim is to fly in a grosser fluid, and to fly is to swim in a subtler. We have only to proportion our power of resistance to the different density of matter through which we are to pass. You will be upborne by the air if you can renew any impulse upon it faster than it can recede.

Professor Pike calls attention to the similarity of the labile equilibrium of the flier and of the fish. He notes the fact that in free-swimming forms, the semicircular canals are well developed; but until the otic labyrinth of the birdman has become more highly developed by change of environment, the eyes must be considered one of the most important of the peripheral sense organs concerned in the very complex problem of equilibrium. Increasing experience with the human machine in aeronautics impresses one very deeply with the feeling that from the beginning the instructions of the chief surgeon to the examining units have been very wise in insisting on good vision, sound eyes, normal muscle balance and strength, stereoscopic vision and ability to recognize colors. In the further classification of pilots, it is also very necessary to test the subjects in regard to their retinal sensitivity.

GOOD SIGHT AN ESSENTIAL REQUISITE IN AVIATION

The value of *acute sight* is so apparent that it seems hardly necessary to draw attention to it as an essential requisite in flying. But no other nation insists on the high standard held by the air service of the United States. It is important in distinguishing enemy planes from those of our allies, in making good landings, and in observing objects of military importance within and beyond the enemy lines. The pilot who sees the enemy first has an enormous advantage in being able to make the first maneuver. Where two planes are approaching each other at the rate of nearly 150 miles an hour (for each plane) one can readily appreciate the importance of good sight. In the tests at the laboratory we have not been able to verify the statements of French observers that the vision of the aviator at about 200 meters increases

practically one-third owing to the congestion of the head in general and of the retina and choroid in particular.

We have found in errors of refraction, in which the focus is preserved by a muscular effort, that there is a falling off in visual acuity during oxygen want, such as one would meet in the air. This is particularly true of hyperopia, in which the accommodation weakens. It is conceivable, however, that increased visual acuity might possibly occur under three conditions:

1. In Europe, where a certain amount of myopia is allowed, there could be an increase of sight in the air owing to a relaxation of the muscle of accommodation.

2. In mild degrees of toxic amblyopia, such as is produced by tobacco, there is a certain amount of anemia of the optic nerve. In these cases, there might be during a flight an increase of visual acuity from the congestion of the intra-ocular tissues.

3. Objects in a rarefied atmosphere are more clearly visible, and vision is improved for a while by the concentration that ensues from the sense of isolation in flying.

In point of fact, the question of change in visual acuity during oxygen deficiency has been under investigation at the laboratory for some months, yet the subjects examined have not been sufficiently numerous to make a statement on the matter authoritative. However, all records up to the present date show that vision has improved in 16.6 per cent., has become worse in 33.3 per cent., and has remained stationary in 50 per cent. The greatest care has been taken to make the tests of vision as accurate as possible by using not only the ordinary Snellen's type, but the Ives visual acuity apparatus, and the instrument devised by Lieutenant Johnson. In spite of all care, however, the elements of practice, memory, fatigue, etc., contribute largely to the possible sources of error.

GOOD MUSCLE TONE NECESSARY

Of almost as much importance as good sight is *good muscle balance and strength*. Otherwise there is a progressive loss of muscle tone as the pilot ascends, resulting in a restricted field of binocular fixation, double vision, and loss of accommodation. Under such conditions there would be difficulty in perceiving and placing an enemy machine and in seeing accurately the baragraph, air speed indicator, revolution counter, compass, inclinometer, drift meter and the numerous other instruments under the eye during flight.

Some time ago I examined the eyes of a pilot who had suffered from two crashes, each accident having been caused by his reading the baragraph incorrectly. The last time, he read the instrument as

showing that he was 1,800 feet above the ground, when in fact he was only 150 feet. In this case, the difficulty was loss of accommodation owing largely to a hyperopia of 1.75 degrees.

In our practical experience, exophoria and hyperphoria are much more serious than esophoria. It has been found that in about 7.37 per cent. of subjects whose muscle strength is normal, there is a decrease in the field of fixation, while this decrease in the field of fixation occurs in 50 per cent. when the muscle strength is subnormal. In these cases, the decrease in the field is more marked in the upper than in the lateral or in the lower portions. In general, one may say that there is a progressive falling off in the muscle strength as the artificial altitude increases.

OTHER VISUAL FACTORS THAT ARE IMPORTANT

The power of *stereoscopic vision* is not considered necessary by enemy nations, and even allied nations do not consider it requisite because its requirement is too stringent. However, its possession is a great asset. This, added to good vision and muscle strength, aids greatly in judging distances, and therefore in making a good landing. For it is harder to make good landings than to do seemingly very difficult stunts in the air. Crashes due to faulty landings are most numerous. In landing, it has been pointed out by Dr. Anderson that the pilot misjudges his distance from the ground and either flattens out too soon and "pancakes," or flattens out too late and strikes the ground at a great angle, usually overturning and wrecking the machine. So far there is no definite falling off in the function of stereoscopic vision during reduced oxygen tension until just before a general break comes.

Good color vision is essential for the pilot in order that he may readily differentiate the markings of planes and distinguish between those of the enemy and those of friends. In landing at night, it is essential to distinguish the signal lights at the airdromes and to locate thereby his own field and hangar. So far our tests do not show any decided change in color vision during decreased oxygen tension.

On account of the very nature and design of the plane, the *visual field* of the airman is contracted irregularly. There is a central portion cut out below and the field is further limited by the wings and interfered with by the wires, struts, etc. However, it is of importance that the remaining field should be acute for catching the motion of an object, an oncoming plane, or landmarks in landing. The art of picking up objects with the peripheral retina, which is probably well developed in the lower animals, is increased in the airman by practice. The famous French "ace," Nungesser, says: "You need eyes all around your head, and after a time you get them."

While our tests of the fields are not based on large enough numbers to be conclusive, in general, we have found a tendency toward enlargement of the fields for white and colors up to 5,000 feet; and from 5,000 to 15,000 feet the fields have remained fairly constant, while at 20,000 feet there is a general constriction of the visual fields in which green suffers the most contraction.

Normal *retinal sensitivity* is important for aviators of all types, but it is a *sine qua non* for those who fly at night. Retinal sensitivity may be tested in two ways:

1. Threshold Sensitivity: By determining the least light stimulus the retina is conscious of by increasing the intensity of the stimulus until the eye is conscious of its existence. This method requires the complete adaptation of the eye by remaining in the dark for at least fifteen minutes. This requires too much time and care.

2. Contrast Sensitivity: The light being constant the subject is tested by seeing the minimum contrast that the retina is capable of recognizing. For practical purposes, the test object is a gray letter on a light gray background, there being thirteen shades of perceptible difference between them. Then one eye is closed and the photometric wedge is passed before the other eye until the letter blends into the background and can no longer be recognized. The point is noted on the millimeter scale of the wedge where this occurs. This is repeated three times for each eye. This wedge, which was devised by Lieutenant Reeves, consists of a layer of gelatin of increasing density of color between two pieces of optical glass. The light transmission has been calculated for each millimeter on the scale and the normal has been established by repeated tests at the laboratory.

PROTECTION OF THE EYES

The question of protection of the eyes of the pilot from wind and bright light is a most important one. The protective goggles should be of good optical glass, free from irregularities, and should afford high transmission. Their contour should permit the widest field of vision possible. The metal portion of the frame should be so constructed that there would be no danger of its being driven forcibly into the eye or face. Nearly all accidents to the eyes and head occur through the head being forcibly thrown against the *fuselage* in making *a bad landing*. Colorless lenses may be worn simply as a protection against the wind. However, the glare encountered in flying above clouds or over sand, snow or water is not only blinding to the vision, but is exhausting to the nervous apparatus by overstimulation of the retina. In the morning, when flying against the enemy, our pilots have to fly with the sun directly in their eyes. In flying away from

the sun, when it is near the horizon, I personally have found that there is a very fatiguing shimmering reflection from the rapidly moving propeller blades. Under these conditions a tinted glass gives a great sense of relief. The best tint for this purpose is a glass with a greenish yellow tint. While giving a high transmission of those spectral rays which are most useful for acute vision, this tint cuts out the harmful short rays and does not change the color of red, greens or blues. It not only protects the sensitive nervous expansion (the retina) from the irritating actinic rays, but it is restful by preventing the necessity of the muscular apparatus of the eye having to adjust the lens to the shorter wave lengths. In addition, this tint actually increases the visual acuity in dust, smoke, mist and fog, by preventing the diffraction and dispersion of light rays by the small particles that produce these atmospheric conditions. It acts as a ray filter, and helps in the detection of camouflage, especially the form produced by paint.

It seems necessary to lay a little stress on the matter of this tint because many rather vague suggestions as to the best tint have been put forward by some observers. It has even been noted that neutral tinted glasses have been suggested because they dim the entire visible spectrum. No airman, however, will wear goggles that materially diminish vision centrally or limit it laterally. An English flier tersely remarked concerning an official goggle: "These are sudden death overseas. You cannot see out of the sides."

The delicate mechanism of the eye indicates as surely as the other organs do the falling off in function during the nervous and physical fatigue of flying and fighting in an atmosphere of diminished oxygen tension, and points to the necessity of proper physical training and expert medical care to prevent the otherwise inevitable staleness of the aviator.

COMMENT

The sense of dizziness and insecurity that one feels on the top of a high building or by rushing water does not exist in the air. Beneath, the earth lies serene and like a beatiful map. The cultivated fields are like bits of brown velvet, and the trees stand out like the Noah's Ark trees of our childhood. It is true that the earth does rush toward one in a nose dive, that it drifts away in a rapid ascent, and that it playfully tilts up in banking, but one's isolation lends a feeling of stability and security. Were it possible to eliminate the whir of the motor, one would experience the feeling of a "peace that passeth understanding."

For their interest and ability in attacking the many necessary problems and in making careful tabulations of results, I desire to express my obligation to, and my appreciation of Captain Berens (the head of the Ophthalmological Department of the Medical Research Laboratory) and his able co-workers.

THE EAR AND AVIATION

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In undertaking to train a man to learn to fly, the Army demands that he be a normal man in good health. Therefore, each applicant for this training is given a careful complete physical examination, including the special senses. The ear examination includes tests of sound-perception, and of the motion-perception of the vestibular apparatus; the regulation requirements demand normal acuity of perception.

The difference between the man on the ground and the man in the air lies in the fact that the former can stand still, the latter cannot. When the flier walks across the field to his plane, all his motor coordinations are concerned with maintaining the proper relation between his body and the element which is supporting its weight — the earth. When he straps himself in the seat before flight, he practically straps wings to his body, thenceforth, until the end of his flight, every motor coordination is concerned with maintaining a proper relation with the new element which is supporting his weight — the air. The only means he possesses of adjusting his relation with the new weight-supporting element is the plane; while flying, all motor coordinations, whether carefully calculated or instinctively performed, are concerned exclusively with controlling the plane. The promptness and efficiency with which motor coordinations are performed depend directly on the acuteness of sensory perceptions.

Rising in the air in an aeroplane is made possible only by rapid motion. Acuity of motion-perception assumes much greater importance to the flier than to the pedestrian, and in order to appreciate the full importance of this, one must have a clear conception of the component senses going to make up motion-perception. Muscle-and-joint sense, splanchnic or visceral sense, kinesthetic sense — all grouped for convenience under the term "deep sensibility," vestibular sense, vision and tactile sense each participate in the composite of general motion-perception.

THE IMPORTANCE OF MOTION-PERCEPTION TO THE AVIATOR

Deep sensibility, on the ground, is practically exclusively concerned with sensing the effect of the pull of gravity on the body; in the air it is also concerned with sensing the effect on the body of two other pulls, that of the plane's propeller, and that of centrifugal force on

curves. Impulses generated by these three pulls coming in via the deep sensibility tract must undergo accurate analysis in the brain and be properly estimated and labeled if confusion and misinterpretation are to be avoided in the sensorium. While such analysis is accomplished by normal individuals, it is only at the exclusion of a certain amount of the more accurate sensing of the pull of gravity. Whereas, on the ground practically 100 per cent. of this incoming information expresses gravity pull, a less percentage of gravity pull is expressed by it in the air.

Vision, possibly the most important of all motion-perceiving senses on the ground, suffers some impairment of its usefulness in the air by reason of the reduction in the number of visible elements in the new environment such as the usual objects making up the landscape. When darkness or cloud further reduces the utility of vision, this sense becomes almost eliminated as a source of guiding information to the flier.

Tactile sense contributes less than any of the other three senses to motion-perception on the ground; to the flier, although insulated by warm clothing and helmet, it is still of value as a source of guiding information.

Vestibular sense suffers no depreciation in utility in the air as compared with on the ground. Its sole function has always been, and continues unaltered in any way to be, pure sensing of motion. In flying, therefore, its function assumes a relatively greater importance than that of the other special senses cooperating with it to furnish the individual with his composite of knowledge concerning motion.

VESTIBULAR TESTS

The motion-perceiving apparatus of the internal ear is subjected to *stimulation* by motion of certain standard quantity and quality, and the results are observed according to uniform standard methods. Two results are noted—a *sensory result,* the subjective sensation of motion, and a *motor result,* involuntary movement of the eyes. When the subjective sensation of motion is in accord with fact, we call it normal sensing of motion; when it is not in accord with fact, we call it "vertigo." The only difference between normal motion-perception and *vertigo* lies in the sensing of motion being in accord with, or contrary to fact. The most practical means of applying motion stimulus is by the rotating chair, since the application of motion in a linear direction, for the period of time and in the intensity necessary to elicit certain standard responses to that stimulus would necessitate apparatus entirely too bulky to be susceptible of practical application under ordinary conditions of office examination. By making use of a rotational motion stimulus instead of a linear motion stimulus, it was

possible to work out a standard means of applying motion stimulus in certain definite quality and quantity in a manner, and by means of an apparatus easily handled in an office. For this reason only, the subject of the tests of the vestibular apparatus is made to experience rotational vertigo. An additional advantage in using the rotating chair is that it applies motion stimulus of a character to produce a more enduring stimulation of the end organs of the semicircular canals.

Motion in a linear direction applied to a fluid contained in a closed semicircular canal is physically incapable of setting up an enduring flow of that fluid, just as rotational motion applied to a fluid contained in a straight canal cannot set up an enduring flow.

NYSTAGMUS PRODUCED BY MOTION STIMULATION

Ewald's experiment long ago determined that involuntary pulling of the eyes in a certain definite direction and plane occurs during the time the fluid in a normal semicircular canal is made to flow in one direction; and that during the time this fluid is made to flow in the opposite direction involuntary pulling of the eyes in the opposite direction occurs. By applying rotational motion, it is possible to reproduce Ewald's experiment in effect, as a test of eye-reactions to vestibular stimulation; and when the character and intensity of rotational stimulus is standardized, comparisons of the results can be made and a normal eye-reaction determined. This motor expression of motion stimulation is nystagmus.

MEASURING VERTIGO

The normal man experiences a sensation of vertigo for between fifteen and thirty seconds after being turned according to standard technic. Evidence of this subjective sensation may be had by *voluntary* or *involuntary testimony; voluntary testimony,* such as "I'm turning to the right," "I'm still turning to the right," etc., during the persistence of the subjective sensation; *involuntary testimony,* such as pointing test and falling. Standard tests make use of involuntary testimony in all cases; occasionally this is amplified by voluntary testimony with advantage. In observing the pointing before turning a very important element in the test can be injected by implanting in the mind of the applicant the definite idea that he is to attempt to determine the location in space of the observer's finger solely by registering in his memory the location of it according to his tactile sense. This can be augmented by having him touch the observer's finger in more than one position (*pointing test*); as, for instance, directly in front of the right hand, come back and touch; then locate again 30 degrees outward and come back and touch; the same procedure in front of the left hand. This implants in his mind the fundamental idea of

being able to orientate himself solely by means of afferent impulses from his tactile end-organs. After standard rotation to the right, for example, normal man experiences certain very definite vertigo, a subjective sensation of turning to the left in the same plane as the rotation for a normal period of time. If the pointing test is carried out during this period of vertigo, instead of succeeding in pointing accurately to the testing finger he executes the pointing in accordance with his subjective sensation of motion. Feeling that he is turning definitely away from the testing finger to the left, he reaches for it to the right. This is normal past-pointing.

METHOD OF APPLYING THE PAST-POINTING TEST

The insulation of the applicant during this test should be as perfect as possible. A black domino mask should be used, absolute quiet should be maintained, olfactory impressions should be shunted out, and he should be left as solely as possible dependent on the information brought to him along the *vestibular tract alone*. The applicant should be definitely instructed before turning that he should not expect a verbal order to touch the observer's finger, raise his hand and come back, and attempt to find it after the turning; he should be practiced before turning in executing his touch, raising the hand, and coming back to find the finger on receipt of the signal from the observer's finger as it comes into the position which it maintains during the test — the observer bringing up his finger into position so as to tap the applicant's finger as a signal for him to execute his pointing without verbal command. It is very important for the applicant's finger to find a finger of the observer when he comes down in search of the finger which is testing him. Otherwise, there is injected into his mind a disconcerting element of dissatisfaction in having failed to find the finger for which he was searching. For this purpose the index finger of the observer's left hand can be held in readiness to furnish the touch necessary to shunt out this sense of failure. In observing the past-pointing after rotation the observer's right index finger should be definitely fixed against the observer's hip, so that visual attention to it on the part of the observer can be dispensed with, the hip rest insuring its remaining definitely where it was when the applicant first touched it in making the pointing test. The observer's eyes can then be free to watch the applicant's finger at the top of the swing. Past-pointing at the top of the swing is just as definitely normal past-pointing as at the completion of return to touch. Many cases compensate after evincing a normal tendency, let us say, to past-point outward with the right hand when they should do so, and subsequently execute a compensatory touch or inward-pointing at the bot-

tom of the return. In such cases the pointing should be registered as that executed at the top of the swing, which is the primary and clean response before it has been altered by the subconscious or conscious compensation effected by other mental processes. Visual attention on the part of the observer to the applicant's hand at the beginning of his downward pointing is of enormous importance, and it should be very carefully observed as part of the standard technic.

APPLICATION OF THE FALL TEST

The fall test is similar. A normal man, on attempting to sit upright after leaning forward during right rotation, feels that he is turning to the left, for instance, and so gives involuntary expression to this sensation by falling to the right on attempting to assume an erect sitting posture.

These tests can be completed in less than four minutes. The neurologist will especially appreciate the extent to which the central nervous system has been examined, and determined to be normal during these tests of the vestibular apparatus.

COMMENT

In view of the foregoing, it is apparent that in flying, motion takes on a much greater importance as regards potential safety or disaster for the individual than it possesses on the ground, and that motion-perception is commensurately of greater importance in the air than on the ground.

Regardless of the actual percentages which would express the shares of vision, deep-sensibility, and vestibular and tactile sense in the total of motion-sensing on the ground, it is established that three of these four are reduced in efficiency by conditions incidental to flying, and the fourth, vestibular sense, is not so reduced, and is therefore of relatively increased importance. It follows that it is of prime importance to determine that men to be trained as fliers possess normal vestibular apparatus. So important is it for the flier to possess normal vestibular acuity of motion-perception that no man should be permitted to begin training as a pilot who has not definitely shown normal reactions to vestibular tests.

This, however, does not end the otologist's responsibility in aviation. It must be borne in mind that physical deteriorations of the vestibular apparatus are always possibilities. Cases have been encountered in which men have gone into the service possessed of normal vestibular sense, and subsequently developed marked impairment of their vestibular function, seriously reducing their flying ability. Re-examination of all fliers at intervals is just as necessary to proper maintenance of the flying service as is the first examination of applicants for admission to this service.

ON THE FOCALITY OF MICROSCOPIC BRAIN LESIONS FOUND IN DEMENTIA PRAECOX

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THE IDEA OF MICROLOCALIZATION

A number of investigators of the mind and its diseases are now pursuing the study of the nervous system along lines roughly summed up in the term microlocalization. But this task must not be conceived narrowly as a task of the histoneurologist or the histoneuropathologist. Microlocalization in the nervous system and especially in the cerebral cortex has threads running to the broadest issues of physiology, embryology and psychology. Yet no one feels that psychologists, embryologists, physiologists, anatomists or even pathologists, in the narrower sense of the term, will solve the problems of microlocalization or even demarcate its problems for solution. When the idea of Flourens that the brain parts were mutually exchangeable in function like so many liver parts, was replaced with the ideas of topographic differentiation which we attach to the work of Hughlings Jackson and of Hitzig, it was as if the naked eye of observation was replaced with a lens of considerable power. The situation now is that this lens of great power, provided by the work of the embryologists, the physiologists and the clinical anatomists, must be replaced with a lens of still greater power, one that will permit us logically to face problems of microlocalization attaching to physiologic complications within the single gyrus. It has become a commonplace that the brain is a congeries of organs. It is not so well understood that each gyrus is a wonderland of structures and functions in which rich results are to be expected from hard but fascinating research.

As we look over the history of these developments, we of course find that Bevan Lewis had, in advance of his time, laid down the idea of cell differentiation within the cerebral cortex, clearly distinguishing the large cells of the motor cortex, for example. In much of the work of Meynert and Flechsig, the idea of microlocalization can be discerned. However, even in the embryological considerations of Flech-

sig, the notion of the gyrus as little more than a functional unit is the prevailing idea. Decades were devoted to the isolation of one neuron after another by ingenious technical methods and to developing the conception of the nervous system as a mass of embryologically and functionally separate units, expressed, for example, in the neuron hypothesis of 1891. Listeners to the lectures of Nissl became familiar with his ideas of the structural and functional differentiation of the various cortical parts.

The idea of microlocalization scarcely flourished to the full in the last decade of the nineteenth century, however, since workers were engaged in assimilating the principles of Weigert concerning neuroglia and in trying to find qualitatively the same sort of lesions in the nervous system that they were finding in other organs. In fact, this search neatly culminated in the establishment in the years 1899-1904 of general paresis as a definite example of chronic inflammation of the nervous system. The pathologist was here trying to find, and succeeded in finding, certain lesions scattered in different parts of the nervous system, and lesions of qualitatively the same sort throughout. Nor, in the rush of new ideas, was the material in general paresis used to the utmost in throwing such light as it might on the problem of microlocalization. Thus, had the world been seriously trying to find out the nature and genesis of mental phenomena and symptoms, it would surely have executed elaborate studies in the distribution of the characteristic paretic exudate, with the idea of correlating these local variations in exudate with processes and symptoms. The issue of such an investigation could have been only positive or negative. As it stands, the situation is doubtful. In fact, it may be confidently doubted whether the paretic exudate itself is at all responsible for many of the characteristic symptoms in paresis, for example, grandiosity, amnesia or even dementia, symptoms which are not found to correspond even roughly with the amounts of exudate discovered in the brains.[1] So far as paresis is concerned, very possibly it was more important to determine it to be syphilitic and to embrace eagerly the opportunities afforded of a Wassermann reaction than to pursue seemingly recondite studies in microlocalization. Meantime the topographic anatomists were laying down the results which the pathologist could at last employ without signal loss of time.

When the interesting and fundamental work of Hammarberg appeared on the histology of freeblemindedness in 1895, it was plain

1. Southard, E. E.: A Comparison of the Mental Symptoms Found in Cases of General Paresis With and Without Coarse Brain Atrophy, J. Nerv. & Ment. Dis. **43**:204, 1916.

that this Swedish investigator had had to spend more than half his time, not on the histopathology of feeblemindedness, but on normal histology. The situation is now greatly improved with the work of Elliot Smith, who showed that even the naked eye will, under proper conditions, detect striking differences between the gyri of different parts of the brain on section, and especially with the work of Campbell, who, after an extensive study of the histology of the different gyri, has offered a valuable atlas with a store of functional comments and speculations.

Even before Campbell, Bolton had laid down exact lines concerning the histology of different parts of the occipital region, and had contributed the idea of visuo-sensory and visuo-psychic regions therein. Similar work has been done by Brodmann, in Germany, who however feels that functional speculations are hardly in point at the present time. Visitors in the private laboratory of Vogt in Berlin some years since must have been impressed with the tremendous elaboration of structures which could be demonstrated in the different parts of the brain, even by so simple a technical method as the method of Weigert for myelin sheaths. For decades, also, the world has been watching the development of the ideas of Ramon y Cajal, whose labors stand not second to those of Bolton, Campbell, Brodmann, and the rest of the topographers.

In fact, the research situation is theoretically so promising in view of the progress along all these lines by workers in different countries, that it is a little surprising that so little neuropathologic application has been made of the results as attained. There seems to be a curious lack of tempo in neuropathologic research. Bevan Lewis' ideas of cortex differentiation came, it would seem, too early to affect the main current of investigation. The work of Donaldson in 1889-1890 on the brain of Laura Bridgman has not been followed up by any considerable series of similar investigations, and the Laura Bridgman work apparently led its author to deeper considerations of growth and development rather than to progress along the line of neuropathology.

ANTILOCALIZING VIEWS OF PSYCHOLOGISTS

Again, late in the nineteenth century, there prevailed the Wundtian psychology. The reader of Wundt's analysis of aphasia, for example, is convinced that, despite the profound distinctions made, the philosopher was no longer a physiologist and set himself the task of anti-localization in the spirit of a system-maker rather than that of an independent seeker after facts and independent interpretations. The idea of the unity of the mind, a very fine-grained and closely interwoven unity, has prevailed in many quarters, perhaps in all quarters, dominating research. To these psychic unitarians it would

have seemed almost a pity if any one could show, for example, an identity of speech processes with processes of the left inferior frontal gyrus. To the conservative wing of the psychic unitarians was added the force of those strictly scientific persons who feel that a fact is a fact and a speculation is necessarily a bad speculation. Thus, for example, if the simpler ideas of Broca concerning speech localization ought to be modified by the modern concepts of Marie, then this is scored as a victory by those holding to the adamantine unity of the mind, on the one hand, and by those who are sceptical of all scientific results in the psychic field of whatever sort.

Added to this situation was the Freudian tendency. Disregarding the truth or falsity of the Freudian contentions, it is clear that his followers are engaged much more in finding satisfactory categories of a logical nature in which to place globar tendencies shown by their patients than they are in conceiving the brain functional lines along which an hysterical dissociation might proceed, a repression be mechanized, or a censor be enthroned.

Inasmuch as Descartes made a laughable error in assigning the seat of the soul to the pineal body, it is best for the modern to "play safe" by failing to notice both the pineal body and the brain itself and to solve the problem either by denying that it exists or by failing to consider it at all. One of these modern worthies assured me some years ago that there was no doubt a correlation between mental processes and brain processes and that, theoretically, the "needle" of demonstrable lesions could be found in the "haystack" of neuronic brain systems, but that for his part he regarded that problem as theoretically solved and desired to get on with something genuine and practical.

Accordingly, the academic psychologists, if we may so term the Wundtians, and the apparently more radical Freudians, have alike little interest in the matter of microlocalization, that is, in the correlation of mental with brain processes, either normal or pathologic.

It is, therefore, almost with a feeling of being alone in the wilderness that one endeavors to work in the direction of neuropathologic correlation; either there is no problem or it is theoretically settled beforehand. A psychiatrist of light and leading asked me one day what, after all, I was about in working along structural neuropathologic lines. Anybody with a logical turn of mind and any capacity for observation ought rather to be busily applying the modern categories of psychopathology to clinical psychiatric and neurologic material. If such doubt of the fundamental value of this kind of work could prevail in the mind of a leading psychiatrist, I felt that I could do no better than bring these general ideas before the Association of American Physicians.

It is, as possibly throwing light on the problems of microlocalization, that the material in dementia praecox struck me as of value. To be sure, the world was full of a rather empty discusison as to whether dementia praecox was an organic or structural disease. Any one who professes to find brain changes in dementia praecox was perforce regarded as a controversialist, engaged in demolishing the pet ideas of some workers who wanted to show that dementia praecox was a disease of maladaptation or a disease with so-called Freudian mechanisms. Let me say, therefore, that to embark on studies of the brain in dementia praecox and to find brain changes therein is not at all to deny that dementia praecox is an instance of maladaptation of the individual to his environment and not at all to deny the possible importance of Freudian mechanisms in the disease.[2]

ANOMALIES IN DEMENTIA PRAECOX BRAINS

In 1906, I began to study the brain problems of dementia praecox and collected first-fruits of that study at the Medical Congresses in 1910[3] and 1913.[4] I then showed that the brains of dementia praecox subjects were extremely likely to show evidences of anomaly, that even when there was no anomaly, there were very likely to be microscopic changes. To be specific, I found twenty-three out of twenty-five carefully studied brains to be significantly anomalous. I do not mean that the anomalies shown were visible the whole length of the demonstration hall, as they are apt to be in brains of the feebleminded; but I mean that the asymmetries and irregularities were of a demonstrable and photographable nature. Friendly critics offered the suggestion that similar anomalies were to be found in brains of normal persons. Unluckily, the brains of normal persons, in large numbers, are not available so far as I know in any laboratory in the world, at least in such a state as to permit proper photographic analysis. However, I think I am able to answer these critics by showing that the brains of subjects of the so-called manic-depressive psychosis show such anomalies in very few instances.[5] Using certain criteria, I found four fifths of my dementia praecox brains to show such anomalies and but one fifth of the manic-depressive brains similarly affected.

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2. Southard, E. E.: The Mind Twist and Brain Spot Hypotheses in Psychopathology and Neuropathology, Psychol. Bull. **11**:117, 1914.

3. Southard, E. E.: A Study of the Dementia Praecox Group in the Light of Certain Cases Showing Anomalies or Scleroses in Particular Brain-regions, Proc. Am. Medico-Psychol. Assn., May, 1910.

4. Southard, E. E.: On the Topographical Distribution of Cortex Lesions and Anomalies in Dementia Praecox, with Some Account of their Functional Significance, Am. J. Insan., October, 1914, and January, 1915.

5. Southard, E. E.: Anatomical Findings in the Brains of Manic-Depressive Subjects, Boston Med. and Surg. Jour., 1915, **172**: No. 4.

But it is one thing for a brain to be anomalous and another for it to be functionally disordered. The underlying hypothesis here is that the anomalous regions of the brain are in some sense weak places therein, such that disease of a toxic or metabolic nature, for example, at puberty, may unfavorably affect the anomalous and poorly constructed region. These considerations I presented with some histologic confirmation at the 1914 meeting of the Association in a paper "On the Direction of Research As to the Analysis of Cortical Stigmata and Focal Lesions in Certain Psychoses."[6] Further reflection on this finding led me to the considerations about tissue decomplication developed at the 1915 meeting.[7]

But it was clear that the few cases of normal-looking brains in dementia praecox formed the crux of the situation, since the critics of material from anomalous brains might properly charge the investigator with inability to cull out the acquired from the inborn lesions. I therefore determined to study with sufficient intensiveness the brains of cases of dementia praecox that showed no anomalies or scleroses. In connection with this study, five brains were investigated, four of them looking in the general direction of dementia praecox and one of them in that of manic-depressive psychosis. These five brains were the residuum of a series of 120 coming from psychoses of all sorts.

Before I could bring the topographic problem into clear relief, I found that in the analysis of these five brains, the problem of parenchymatous versus interstitial lesions stood out. At the 1916 meeting I presented the conception that in the nervous system there should be a dissociation of lesions somewhat similar to that in the kidney.[8] To be sure, the parenchymatous and interstitial lesions of the kidney are, as is well known, often if not almost always commingled. But the fact that the lesions in these two types of renal tissue are so commingled in a given case militates not at all against the idea that there are, roughly speaking, two kinds of nephritis — parenchymatous and interstitial. The same theoretical situation holds in the nervous system. I found that parenchymatous and interstitial lesions could be dissociated and combined in the nervous system, much as similar lesions could be dissociated and combined in the kidney. To be sure,

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6. Southard, E. E.: On the Direction of Research as to the Analysis of Cortical Stigmata and Focal Lesions in Certain Psychoses, Tr. Assn. Am. Phys. **29**: 1914.

7. Southard, E. E.: Advantages of a Pathological Classification of Nerve Cells, with Remarks on Tissue Decomplication as Shown in the Central and Cerebellar Cortex, Tr. Assn. Am. Phys. **30**: 1915.

8. Southard, E. E.: On the Dissociation of Parenchymatous (Neuronic) and Interstitial (Neuroglia) Changes in the Brains of Certain Psychopathic Subjects, Especially in Dementia Praecox, Tr. Assn. Am. Phys. **31**: 1916.

the parenchyma of the nervous system was a parenchyma composed of neurons and their adnexa and the interstitial tissue of the nervous system was complicated by the fact that a great deal of it is neuroglia tissue, embryologically different from the interstitial tissue of the kidney. Nevertheless, it is well known that many of the properties of neuroglia of ectodermic origin are similar to the properties of mesodermic interstitial tissue. The alterations of the mesodermic interstitial tissue also existent in the nervous system are of far less consequence than those of the neuroglia tissue. The one case of manic-depressive psychosis, intensively examined, failed to show convincing degrees of parenchymatous lesion, but the dementia praecox case had well-marked parenchymatous disorder, that is, varying degrees of cell loss, to which the interstitial reaction, that is, gliosis, was found to be not at all proportionate. The result of this study seemed to be that parenchymatous disorder, namely, cell losses and interstitial disorder, namely, gliosis, must be investigated separately if we are to make headway in this group of cases. Thus it would be decidedly unwise to argue from the data of neuroglia preparations that the gliosis of such and such an area was an indicator of parenchymatous loss. To be sure, the gliosis is probably an indicator of something of general or local significance in the brain. But no facile application of the principle suggested by Weigert's neuroglia work could safely be made. Even if gliosis, as a rule, signifies some degree of wear and tear on the part of the parenchyma of the part affected, yet there was no good evidence that the gliosis was at all proportionate to the parenchymatous wear and tear.

STRATIGRAPHICAL ANALYSIS OF THE CEREBRAL CORTEX

Having thus shown that the brain conditions roughly corresponded to, for example, renal conditions, and that the histopathologic analysis of injured brain tissues must look in both these directions in search of successful correlations, I proceeded to a stratigraphical analysis of the finer cortex changes in these brains, presenting results at a meeting of the American Neurological Association.[9] I tried to study separately the nerve cell losses, on the one hand, and the gliosis (including satellitosis), on the other hand, and then to learn whether the character of these changes in the upper and lower layers of the cortex was of any functional significance. For convenience, I wish to term the upper layers of the cortex supracortical and the lower layers infracortical. In fact, it might be well at times to speak of the supra-

9. Southard, E. E.: The Stratigraphical Analysis of Finer Cortex Changes in Certain Normal-Looking Brains in Dementia Praecox, J. Nerv. & Ment. Dis. **45**:97, 1917.

cortex and the infracortex. The comparative anatomists seem to have demonstrated the importance of some such distinction and the literature has for some time contained references to the so-called suprastellate (supragranular) and infrastellate (infragranular) layers of the cortex. Omitting controversial details, it appears that almost all workers are committed to the idea that the majority of the supra-cortical structures are of more recent evolution than the majority of the infracortical structures. As many of the mental functions in man are of recent evolutionary origin and as all signs point to the cerebral cortex as somehow engaged in these processes, it seems natural to assume that the supracortical layers, or what we may term the supra-cortex, are the basis of many of these higher psychic functions. With the same plausibility, we may argue that the infracortical layers, or what we may term the infracortex, is the basis of such mental or quasi-mental functions as are found in those animals possessing an infracortex and not yet a supracortex.

All these interpretations are independent of any topographic conceptions, and for the purposes of generalization one neglects for the moment the important distinction of the archipallium and neopallium, developed by Elliot Smith.

Taking the whole cortex, by and large, modern work seems to me to invest the supracortex with higher psychic functions than the infracortex.

Now in a disease like dementia praecox as psychologically formulated by Bleuler, we find the main feature to lodge in what Bleuler terms schizophrenia. This most valuable term expresses what one might call "split-mindedness" or mental dissociation. Much of modern psychology, whatever may be said to the contrary, is founded on the work of the associationist school of, for example, John Stuart Mill. We should hardly get on without some of Mill's so-called mental chemistry. Well, for better or worse, associative processes must have their obverse in dissociative processes, and the measure of mental dissociation is the degree of schizophrenia in Bleuler's sense. Kraepelin himself, who, on purely clinical grounds of a combination of certain symptoms in certain ways, laid down the conception of dementia praecox, has so far admitted the validity of Bleuler's conception of schizophrenia as to use the term schizophrenic very frequently in his description of patients. For one of the most exquisite examples of schizophrenia, namely, the finely divided cleavage of speech known as *Wortverwirrtheit*, Kraepelin has constructed the term *schizophasia* on the analogue of schizophrenia.

We mean then by schizophrenia a process of mental dissociation, a psycholytic or ideolytic process. The cleavage may lie between the intellect and the emotions, such that the emotions do not at all fit the

ideas entertained by the patient. Or the cleavage may lie between the emotions and the will, and a bizarre-looking conduct may fit a certain quasi-normal state of feeling. But the cleavage is not necessarily so elective and total. The cleavage may be within some particular train of thought. Here is schizophrenia in its best display. Instead of the regular train of thought, we may have a train of thought like a telegraph despatch, or even a train of thought suggesting in its obviously inappropriate sequence a cipher or a set of types reduced to pi. But absolutely pied thinking is not the rule and the so-called word salads are often but passing phases in the development of a dementia praecox course.

MANY EFFECTS OF MENTAL DISSOCIATION PROBABLY CORRELATED WITH SUPRACORTICAL DISEASE

Here is not the place to expound or to describe schizophrenia. Inasmuch, however, as many of the schizophrenic effects that strike the observer as so bizarre in dementia praecox thinking are probably correlated with the operations of the outer layers, that is, of the supracortex itself, we have to inquire whether cases of this order show lesions preferably in the supracortex. Of my four cases of dementia praecox, all showed lesions in the supracortex in the nature of cell loss and of more or less disproportionate gliosis, except one case. This case was one approximating the so-called paranoia, a disease perhaps allied to dementia praecox, but often running years or throughout life without any of the bizarre psycholytic, schizophrenic, thought-splitting phenomena here under discussion. For paranoiacs of this rare description (there may be in a dozen institutions in Massachusetts at this time not more than twenty-five or thirty of these particular cases), present quasi-normal appearances that have been described sometimes as psychic malformations and often give the impression of ability to fit in to a reconstructed world with the patients in the center as Kaisers or I. W. W. chiefs therein. In short, many of these paranoiacs, victims of the severest and most intractable psychosis known, are nevertheless without a trace of mental splitting such as I have hinted at above. And, in fact, the paranoiac in question showed no signs of mental dissociation, but rather showed signs of what might be termed a hypersynthesis of such facts in her environment as fitted her morbid ego and her jealousies. What I am getting at is that the psychopathologic analysis of this case of paranoia precisely did not demand any evidence of supracortical disease, in fact, had there been supracortical disease of any moment, we should have wondered whether there had not been some disintegration of the patient's personality, at any rate at the close of her life. It is interesting that this particular paranoiac did show some infrastellate dis-

ease which, as will be mentioned below, I regard as correlated with the auditory hallucinations which she showed.

The other three cases intensively examined (I may recall that notes were made as to different types of cell loss, gliosis, satellitosis, vascular changes, etc., for each layer in each of from twenty-five to thirty areas of the cortex in each subject) showed signs of supracortical disorder as well as of infracortical disorder of varying degrees in different parts of the cortex, and all three of these cases showed signs of schizophrenia. This evidence is at least suggestive that supracortical disorder is necessary in schizophrenia. I felt satisfied in my own mind, from the results of the work, that not only is the cerebral cortex the proper study of the psychologist and the psychiatrist, but that the supracortex is in a still more intimate sense the proper study of the psychologist or psychiatrist who has to deal with the higher functions of what may be called psychic association or synthesis. To my mind, such studies, if in future confirmed, will throw an important added light on the problems, already partly illumined by comparative anatomy.

Let me insist here, if it is not superfluous, on the fact that I am not proposing an hypothesis to the effect that every time a mental split occurs, a cell drops out of the supracortex. I do not even see in my mind's eye a dendrite dropping off a supracortical cell to signalize the cleavage of an idea. There is very properly much fun to be made of workers who regard ideas as fine transparent substances poured in and out of nerve cells as wine in and out of goblets. Aside from the problem of parallelism and interactionism suggested by the figure that regards brain cells as vehicles for ideas, my own contentions deal rather with the observational facts. I would regard all gliosis as merely indicating and not defining the type of cortical disease in question and I should regard the nerve cell losses or other changes as likewise nothing but indicators of the kind of thing going forward, or perhaps as indicators that something or other is going forward in the injured tissue. To be sure, I would think that destructive brain changes would be more likely to be associated with mental dissociation (with schizophrenia, gliosis) than with other types of synthetic or redistributive mental processes. Supracortical neuron destruction, to put the whole matter in a formula, is to my mind correlated with schizophrenic processes. What, you may well ask, is to be correlated with hypersynthetic, falsely synthetic or redistributive mental processes of the mind twist sort? For the present I, for one, have no idea what cortical process corresponds to these nondestructive, morbid psychic processes. Mind lack and mind loss *should* correspond with cell lack and cell loss. What we term figuratively mind twist, for example, false reasoning without loss of sensory intake and power, without

loss of memory images, without loss of power of expression, without any evidence of coarse loss of function, remains as a process not readily statable. Perhaps we must fall back here on the idea of physicochemical changes and of anomalous distributions of energy in normal neuronic systems. But these are speculations so remote from observational facts that so far as I can see they cannot even do the observer any harm.

CORRELATIONS OF HALLUCINOSIS AND CATATONIA WITH INFRACORTICAL DISEASE

Besides schizophrenia there are other bizarre effects in dementia praecox. Perhaps the strangest thing in the world is catalepsy. Catalepsy, catatonia, *flexibilitas cerea,* are not infrequent symptoms in many cases of dementia praecox. They all have the character of muscular hypertension somewhat suggestive of hypnotic effects or again of the effects of drugs on the muscular system. Sometimes the phenomenon of negativism and resistivism reminds one of the Sherringtonian experimental effects showing innervation of antagonistic muscle groups. Possibly these processes are to be explained on some general line as schizophrenia; possibly they are due to some kind of lysis; some workers are inclined to use the concept of inhibition very freely in the attempt to explain them. They are often a transient phase recurring again after comparatively normal intervals in a schizophrenic patient, and it seems impossible to evoke them by any form of stimulation of the patient.

In a general way, such conditions as catalepsy seem a good deal more like phenomena producible in lower animals than would schizophrenia. Some of the hypnotic or pseudohypnotic appearances in lower animals roughly resemble the catatonic effect. It was in a case of catatonia that Alzheimer first stated that there were nerve cell changes in dementia praecox, and it will be remembered that he placed these changes (chiefly gliosis) in the lower layers of the cortex. To a certain extent, my own investigations here confirm those of Alzheimer; at all events, in the cases showing catatonia there were lesions in the infracortex.

Another symptom not at all so bizarre as schizophrenia and catatonia is hallucinosis. Hallucinations are rather quasi-normal effects that the normal person rather readily understands and that occur in a great number of mental diseases. Hallucinosis is in short a far less pathognomonic symptom for dementia praecox than is either schizophrenia or catatonia. Many forms of hallucination seem to be of so simple a nature that they would well be elicited in the lower animals, could we only get at the psychic interiors of the lower animals to learn their mental contents. A priori, therefore, it seemed to me that

the disease process underlying hallucinosis ought to be in the infracortex rather than in the supracortex, and there was some confirmation of this idea in the case studied. I mentioned in the foregoing the fact that late in the disease, the paranoiac patient developed auditory hallucinosis. She showed infracortical cell loss of a mild but distinct degree. It will be remembered that the brain of this case was the most nearly normal of all the brains so far studied in the whole series.

The stratigraphical analysis of these brains accordingly proved very alluring. I seemed to get evidence that the supracortex was a region whose disease might well spell schizophrenia, whereas the infracortex was a region whose disease was related with lower level symptoms, such as catatonia and hallucinosis. The supracortex and the infracortex would then be regions of differential interest for the psychiatric investigator, who would seek in the supracortical region for evidences of higher intellectual disorder in the field of association, combination and abstraction, and in the infracortex for evidences of lower forms of mental disorder, such as catalepsy and hallucinations. I would not stick on the question of higher and lower functions at this point. Catatonia may well be a far more complex matter than many forms of intellectual dissociation; I call it lower because it seems to me that a simpler organism could show catalepsy rather than disorders of combination and abstraction in the intellectual field.

I have recently reviewed the cell findings in the different cortical areas, assuming that I should find rather suggestive topical correlations between special kinds of symptom and special loci. I assumed that a priori no one would be likely to hunt for the source of auditory hallucinations in the smell zone as defined by the comparative anatomists, and that one would hardly be likely to look for the basis of visual hallucinations in the superior temporal gyrus!

Perhaps in accordance with the opinion of the learned psychopathologist above mentioned, it is a priori certain that in point of fact auditory hallucinations have their basis somewhere in the temporal lobe and visual hallucinations somewhere in the occipital region, and why undertake a superfluous task of setting out exactly where and under what conditions they occur? We ought to be helped greatly in this matter by the focality of lesions in dementia praecox.

TENDENCY TO LOBAR AND LOBULAR FOCALITY OF LESIONS

In the beginning I had been attracted by the fact that there was often a lobar or lobular hypoplasia, atrophy or sclerosis in these brains. In fact I had tried, reasoning from the gross data alone, to draw tentative conclusions as to the main lines of functional differentiation in the symptoms of dementia praecox.

Noting how difficult was the distinction between inborn anomaly and acquired lesion and how uncertain one might be that a given hypoplasia had anything to do with a given disorder of function, I felt that I ought perhaps to investigate cases without gross lesions.

Now one of the most generally significant results of this intensive examination of numerous areas and all layers in dementia praecox brains is that there is a certain focality in the microscopic lesions. I still find the focality to be rather a lobar or lobular one than an intragyral focality. To be sure, my colleague, Dr. H. I. Gosline, has made some interesting observations on some exquisitely focal lesions of intragyral distribution, possibly related with tuberculosis, in certain dementia praecox brains.[10] Gosline has endeavored to show that the situation of these lesions (demonstrable by fat strains) is such as to fit with my own older contentions as to the relation of certain symptoms to particular regions. Notably Gosline endeavors to confirm my idea of the correlation of catatonia to postcentral lesions. My own work, as here reported, deals not with results of fat stains, but with the results of the study of cell losses by the ordinary tinctorial methods for determination of tubercle, at least with nerve cells (cresyl violet after formalin fixation). I have tried to show the cell losses thus made out as a little more reliable than the fat-stained cells and deposits that Alzheimer, Cotton and Gosline have used. Using the methods of these observers, I obtain too rich a display of lesions, as a rule, to permit correlation.

The kind of focality of lesions which I believe to have demonstrated in these brains is not intragyral, but lobar and lobular, or in certain cases a focality of lesions affecing the whole gyrus. By and large in these brains, as one examines the different layers within a gyrus, the layers are apt to show throughout the gyrus the same kind of lesions, whether gliosis or cell losses. In short the focality of these lesions is not the focality of tubercles, tumor masses, glanders lesions or exudative lesions. It is rather a focality such that, for example, the postcentral gyrus on one side is affected in a certain way throughout the gyrus with such and such layers homogeneously affected. The postcentral gyrus of the other side is relatively normal.

What now are the functional results of a study of the topographic distribution of the lesions just mentioned? Can we by focalizing attention on certain gyri discover functional correlations of lesions with certain symptoms?

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10. Gosline: Paresis or Dementia Praecox? Boston M. & S. J. **177**: No. 10, 1917.

The functional correlations of my dementia praecox studies published in 1910 and 1914-1915 were summed up from the topographical point of view as follows:

1. Delusions are, as a rule, based on frontal lobe disease.

2. Catatonic symptoms are, as a rule, based on parietal lobe disease.

3. Auditory hallucinosis is, as a rule, based on temporal lobe disease.

Re the frontal lobe correlation with delusions, I found an exceptional group of delusional cases without frontal emphasis of lesions; but I found a plausible reason for these exceptions. On analysis, the nonfrontal cases of delusion formation turned out to be cases with a tendency to what may be termed hyperphantasia, that is, to an elaboration of phantasies not more than half believed, or at any rate not fully believed, by the patient. It is clear that from what we know of the probabilities of localization in the brain, both from a comparative and anatomoclinical point of view, the parietal lobes might plausibly be implicated in the function of imagination, and that parietal disease might well be attended with functional disorders of imagination, such as overimagination or what is here termed hyperphantasia.

It is plausible to argue that because the parietal tissue, newly evolved in the higher animals, lying between the tactile postcentral region and the visual occipital region and the auditory temporal region, should be a tissue related with apparatus for combining these sensory data, a tissue which might unobjectionably be termed a center for combining percepts and concepts involving two or more forms of sensation or perception. Whatever the merits of this a priori contention, at all events I found a tempting correlation of phantastic delusions with parietal lobe atrophy.

I summed up the anatomic situation as follows:

> On the whole, the correlation between delusions and focal brain atrophy (or aplasia capped by atrophy?) is very strong, particularly if we distinguish (1) the more frequent form of delusions with frontal lobe correlations from (2) a less frequent form with parietal lobe correlations.
>
> The nonfrontal group of delusion formations, the writer wishes to group provisionally under the term *hyperphantasia*, emphasizing the overimagination or perverted imagination of these cases, the frequent lack of any appropriaate conduct-disorder in the patients harboring such delusions, and the a priori likelihood that these cases should turn out to have posterior association center disease rather than disease of the anterior association center. This anatomic correlation is in fact the one observed.

My previous work had also suggested a possible correlation between catatonic phenomena and parietal (including postcentral) disease. Ten of fourteen definitely catatonic cases yielded gross lesions in the

parietal or other post-rolandic regions. Of the remaining four, two, negative in the gross, proved to be microscopically altered in the parietal region, and there were indications of a correlation in the remaining two cases. It must be remembered with respect to correlation that I am using the term "catatonic" here as the name of a symptom. I am not offering a correlation between anatomic or microscopic lesions and the catatonic form of dementia praecox.

For example, the symptom *flexibilitas cerea* is not necessarily an indicator that the victim belongs in the so-called catatonic form of dementia praecox, despite the fact that *flexibilitas cerea* is one of the prettiest examples of catatonia ever described. Four of the five cases in the 1914-1915 series that showed *flexibilitas cerea* had parietal anomalies or atrophies, and the fifth case, though it was entirely negative in the gross, was one which showed an extreme degree of satellitosis in the postcentral region examined microscopically. These observations and certain a priori considerations led me to formulate the idea that catatonia, and particularly *flexibilitas cerea,* was a form of disorder of kinaesthesia.

Re the correlation of auditory hallucinosis with temporal lobe lesions, it is easy to see that such a correlation ought to exist if any gross correlations at all were expected. In point of fact, nine of my twelve hallucinating cases have had temporal lobe atrophy or aplasia. One of the three remaining cases had ample microscopic changes in the temporal lobes; one was clinically somewhat doubtful and, in fine, only one of the twelve hallucinating cases could be safely said to have neither gross lesions nor important microscopic lesions in the temporal area.

To sum up then: (1) we expect frontal lobe lesions in cases of delusion formation, provided that the delusion formation is not of the phantastic and overimaginative sort, whereupon parietal lesions would be expected; (2) we expect parietal lesions associated with catatonic symptoms, and (3) we expect temporal lobe lesions in cases of auditory hallucinosis.

ANALYSIS OF FOUR CASES

Accordingly, I have collected the microscopic data in the four cases at present under discussion under these heads—frontal, parietal and temporal. For convenience I have divided the cortex into three portions — frontal, parieto-occipital and temporosphenoidal. The following table indicates the extent of nerve cell loss and of neuroglia proliferation, separately in the three regions mentioned:

It is clear from inspection of the table that Case 1 (10.9) stands out as a case in which the parenchymal disease is especially parieto-occipital, since in ten loci seventeen instances of nerve cell losses in

different layers were found. Here then should be a case with catatonia unless perchance the lesions in the parieto-occipital area should be exquisitely occipital and not affect kinesthetic areas. In point of fact the lesions enumerated are all in the postcentral, superior and inferior parietal areas and are especially marked in the inferior part of the postcentral gyrus and in the superior parietal region on both sides.

SHOWING EXTENT OF NERVE CELL LOSS AND OF NEUROGLIA PROLIFERATION

	Case I (10.9) Duration 14 Yrs.	Case II (12.41) Duration 10 Yrs.	Case III (12.47) Duration 2 Yrs.	Case IV (11.36) Duration 20 Mos.
Frontal loci	9	9	9	6
Nerve cell losses	5	44	35	34
Neuroglia proliferation	7	8	4	3
Parieto-occipital loci	10	9	10	7
Nerve cell losses	17	47	54	19
Neuroglia proliferation	8	3	2	8
Temperosphenoidal loci	10	10	10	6
Nerve cell losses	9	48	50	25
Neuroglia proliferation	5	9	1	0

This patient was one that developed characteristic catatonic symptoms, including *flexibilitas cerea* and attitudinizing in the last two years of her life. She also had auditory hallucinosis in those years, and showed, as the table indicates, a number of parenchymal losses in the proper area, especially in the superior temporal gyrus. Both the parietal and the temporal lesions were largely infracortical in distribution, in accord with the argument mentioned in the foregoing as to the infracortical origin of catatonia and hallucinosis. It will be noticed from the table that there were comparatively few lesions in the frontal region. The case was one of delusions of jealousy and might have been expected to have shown frontal lesions, which, however, were not greatly in evidence. However, on closer analysis of the delusions, it will be found that they are of a synthetic character and not of a schizophrenic character. They are quasi-normal, and it is not easy to conceive just what histologic basis such delusions *ought* to have. At all events none of any consequence were found, and the frontal region remains practically destitute of any parenchymal loss and has exceedingly slight evidence of gliosis. Accordingly we may suppose that we are getting histologic evidence in this case merely of the terminal hallucinosis and catatonia and not of the essential paranoia of the patient.

If we turn to Case 2 (12.41) we find a totally different situation. The amount of parenchymal loss, as indicated by the number of loci, is far larger than in Case 1 (10.9). In fact, there are four times as many foci affected, and the lesions are scattered throughout all three regions — frontal, parietal and temporal. There are relatively more parenchymal losses in the frontal region than in the temporal region and relatively more in the temporal region than in the parietal region.

If we took these data on their face value, we should say that this case ought to be predominantly delusional, but also hallucinatory and catatonic.

There was some question whether the patient was not slightly feebleminded to start with. However, her command of theological verbiage was large, and she was always self-supporting up to the time of her psychosis. My point in mentioning this query is that very possibly some of the apparent parenchymal losses are actually due to an initial lack of cells. The interpretation of an initial *lack* of cells in any of these areas would of course look in a different direction from that of an initial *loss* of cells. An initial lack in frontal cells might not at all suggest delusional tendencies; an initial lack of superior temporal cells likewise might have nothing to do with auditory hallucinosis. And a simply constructed parietal mechanism would not necessarily entail disorders of kinesthesia with the production of catatonia.

But taking the parenchymal deficiency as signifying initial *loss,* let us inquire what the symptoms of this case are. Was it predominantly delusional? She showed hallucinations of a doubtful but probably of a hypnagogic visual nature. It is not clear that she ever had auditory hallucinations. The appearance of parenchymal loss has proceeded in all these areas to a marked degree, so marked, in fact, that it is rather surprising that there was no gross evidence of brain atrophy (the brain weighed 1,130 gm., possibly a slight reduction from the normal weight; the patient was cardiac and there was such a condition of infiltration of the brain tissue that we can *post hoc* readily believe the brain was slightly and diffusely swollen). In short, the lesions in this brain are so numerous and widespread, and so affect both the supracortical and the infracortical regions that correlations of the nature here attempted are impossible. One can find a correlation between almost any symptoms and some properly situated lesion in this case. The patient was deluded, hallucinated and catatonic, and had frontal, temporal and parietal lesions.

Let us, for the sake of argument, regard the frontal lobe delusion correlation as established; let us regard the parieto-occipital correlation with "feelings of being hypnotized" and the "black cat jumping

over a pitcher" as indicators of disease in the parieto-occipital or occipital areas. How then shall we interpret the absence of auditory hallucinations? Without invoking the poverty of clinical observation and the fact that the patient may have kept auditory hallucinations to herself (she was, in point of fact, often engaged in vituperative language, some of which may have been of hallucinatory origin or of a responsive nature), we must be interested in the fact that some of the temporal lesions shown are exceedingly heavy and affect both the supracortex and the infracortex. Suppose infracortical, temporal lobe lesions of a nature suitable to produce hallucinations (we are still ignorant just what sort of lesion ought to produce hallucinations), would it be too speculative to suggest that the existence of severe supracortical lesions might well interfere with the proper combination and abstraction of the infracortical data in such wise as to produce conscious hallucinations? That is to say, the total supracortical and infracortical mechanism may be conceived to be so altered that, though the conditions for hallucinosis are present in the infracortical zone, the hallucinations are not purveyed through lack of finer connections with the higher psychic apparatus mediated by the supracortical layers. Naturally, I do not wish to claim more than speculative value for such considerations. It is along these lines, however, that I feel that much important correlation will be secured in future.

If we inspect the table of local distribution of lesions in Case 3 (12.47), we find conditions approximating those of Case 2 (12.41), although the duration of Case 3 is far less than that of Case 2. We find here that the parieto-occipital region has numerous lesions and slightly in excess of lesions, also numerous, in the frontal and temporal areas. The case was a catatonic one and in fact, showed both *flexibilitas cerea* and catatonic stupor, and would probably be classified as a case of catatonic dementia praecox. It appeared that she had auditory hallucinations which she tried to keep out by covering her head with her arms; but the content of these hallucinations was never made out. An attitude of apprehensiveness, an early phase in which she constantly repeated the words "Father Patterson," "Father Patterson," led us to the idea that she had delusions of persecution, or else that she was extremely apprehensive and threw a delusional coloring over every-day features of the environment. The most pronounced regions of cell loss were in the infracortical portions of the parietal and temporal regions.

When we come to the analysis of Case 4 (11.36), we find that the parieto-occipital lesions are far fewer in number, and that the case is more one of losses in the frontal and temporosphenoidal areas. This case, therefore, should show delusions and possibly auditory hallucinations. She never showed convincing catatonic symptoms,

although she showed a marked mania and hyperkinesis somewhat suggestive of manic-depressive psychosis. She showed characteristic auditory hallucinosis, and it appears that most of her antisocial acts of a mischievous and silly nature were based on these hallucinations. That she showed definite delusions, for example, of persecution or of poisoning, is doubtful. We know little of her history immediately after the onset of mental symptoms which followed confinement in a hospital for consumptives. Throughout her period of observation in a hospital for the insane, she showed elation, erotism, mischievousness and silliness somewhat suggestive of manic-depressive psychosis and again somewhat suggestive of the elation of certain paretics. The cell losses in frontal region were numerous and both supracortical and infracortical in distribution. It is interesting that of all four cases, this one was the case which showed a marked myelin sheath disorder, a disorder so marked as somewhat to suggest the disappearance of fibers in paresis. The supraradiary fibers were absent in all the frontal regions examined and there was a thinning of fibers in the white matter underneath. In short, the disorder in this case was much more than a fine disorder of minor cell mechanisms and approached the more general and globar disorder of paresis, though of course without exudation. On some such lines I would be tempted to try to explain the absence of definite delusions except those based on hallucinations and irritability. I should be tempted to regard the frontal lobe lesions as of such degree that we might think of the case as one that had lost its frontal inhibitions. At the same time, it must be remembered that no coarse atrophy of the brain had supervened, unless we regard the brain weight — 1,140 gm. — as demonstrating brain atrophy.

SUMMARY

Thanks to the work of Elliot Smith, Bolton, Campbell, Brodmann, Ramon y Cajal and others, the neuropathologist can now afford to attempt finer functional histologic correlations in the field of mental diseases, thus aiding in the problems of microlocalization. The anti-localizing tendencies of the Wundtians and the interest in merely logical categories taken by Freudians should not interfere with progress in microlocalization. Dementia praecox, for example, can be called a matter of maladaptation of the patient to his environment or of the patient to himself and also a disease characterized by cortical changes.

Previous work had shown anomalies in a high proportion of dementia praecox brains and in a correspondingly low proportion of the brains of manic-depressive subjects. These anomalies may well be interpreted as weak places in these dementia praecox brains, and the

brains in fact are apt to show scleroses and atrophic processes over and above the anomalies. But certain perfectly normal-looking brains in dementia praecox also show the same microscopic changes in lesser degrees than are found in the anomalous sclerotic and atrophic brains. The problem of the present communication has been to work out the focality of these microscopic lesions in a few normal-looking brains studied with unusual intensiveness. In the same series of brains, work of previous seasons had shown a dissociation of parenchymatous (neuronic) and interstitial (neuroglia) changes, indicating a tendency on the part of cortex pathology to resemble the pathology of the kidney. But the majority of brains show mixtures of the parenchymatous (neuronic) and the interstitial (neuroglia) lesions. Recent work in comparative anatomy indicates the rather fundamental importance of distinguishing the functions of the upper cortical layers (what may be called the supracortex) from the functions of the lower cortical layers (what may be called the infracortex). The finer processes of mental dissociation (schizophrenia) *ought* to be correlated with lesions of the supracortex, and such lesions were found in cases with evidence of schizophrenia.

On the other hand, in a case of delusions characterized by no splitting (schizophrenia) whatever, but rather by a process of overelaborate synthesis, there was no evidence of supracortical disorder and in fact, no proposal can be made for any histologic correlate with this process of oversynthesis.

Other processes equally characteristic of dementia praecox, but logically far simpler in their make-up, such as auditory hallucinosis and muscular hypertension (catatonia), received suggestive correlation with processes in the lower layers of the temporal and parietal regions, respectively.

As far as the tissues of these four cases go, there is little or nothing inconsistent in the findings with the hypothesis that ordinary (nonphantastic) delusions are correlated with frontal rather than with otherwise situated lesions; but the supracortical type of delusions found in certain long-standing paranoiacs whose fine mental processes run in a quasi-normal manner, find no special correlation in any region, and the probable lines on which this problem is to be solved remain obscure.

As for auditory hallucinosis, the work seems to afford the expected correlation with temporal lesions. In one case, however, temporal lesions of considerable severity were not attended in life by hallucinations of hearing, but in this case there was also a severe supracortical disease of the temporal region, and it may be that for the production of hallucinations, some congress is necessary between the activation of the supracortex and infracortex, respectively.

In previous work on this series, the brains had indicated a postcentral and superior parietal correlation for catatonia whose muscular hypertension was accordingly regarded as very possibly a kind of morbid kinesthesia. Present work suggests that the anatomic correlate is not merely to the postcentral and parietal regions, but still more specifically to the infracortical parts of these regions.

It may be suggested that the lesions found in samples of tissue in the postcentral, superior parietal, inferior parietal and superior temporal regions indicate a certain systemic tendency in the underlying processes. For these lesions were bilateral and occurred, as it were, in two continuous sheets of tissue on both flanks of the brain in one of the best defined of our cases; these flank lesions were not attended by any similar lesions of the frontal, precentral, occipital and lower temporal and smell regions. The nature of a process which could mildly affect nerve cells and neuroglia on two sides of the brain and also specially affect the infracortical rather than the supracortical portions of these affected sheets of tissue remains a mystery. It is perhaps no greater mystery than that which attends the distribution of lesions in the spinal cord of pernicious anemia. It remains unsettled whether these lesions are secondary in point of time to a noncell-destructive phase in the disease, or whether the lesions of which these microscopic effects are indicators began *pari passu* with the symptoms — that is, it remains a question whether we are dealing with the excess wear-and-tear process of cell mechanisms morbidly employed or whether the morbidity of neural function is an exact equivalent of the neuronic and neuroglia morbidity.

THE HISTOGENESIS OF MULTIPLE SCLEROSIS*

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(This article is concluded from page 64 in the January number)

The so-called "areolar areas" show a distention of the perivascular glia network with the glia relatively unaltered. Large spaces are thus formed, some of which open into adjoining meshes by breaking through the septa separating them; the broken ends appear projecting into the large meshes which have become more or less distended into one large space. Within this area the myelin sheaths have disappeared and in most cases the axis cylinders also, or they are still indicated by small, slightly stained, round or ovoid masses of the margin of the spaces. Most of the spaces are empty, though some of them contain small irregular granules and portions of fibers. The constituent elements of the vessel walls are more or less separated; in some of the vessels wide spaces are formed between the connective tissue trabeculae of the adventitial sheath. These spaces frequently contain more or less debris.

An area of more or less dense glia tissue surrounds this space forming a definite transition zone, the meshes of which contain numerous epithelioid cells. The blood vessels of the peripheral zone show a marked accumulation of nuclei in the adventitial sheaths. The myelin sheaths show varying degrees of disintegration which is indicated by the variation of color in the Bielschowsky preparations. In much of the zone it is entirely absent. In the most peripheral part of the transition zone there are large protoplasmic glia cells and an increase in the nuclei belonging to the small glia elements.

It is evident that the "areolar areas" of this type are the result of a more rapid and intense process, that is, an exudate, the result of a stasis from the blocking of a blood vessel, which is followed by a rapid degeneration of the nerve elements and a compensatory reaction in the neuroglia tissue of the transition zone. Many of these areas are not unlike those resulting from an arteriosclerosis softening, in which there is a central space with remnants of the blood vessel wall and granular debris with an areolar transition zone of denser neuroglia tissue in the meshes of which are large epithelioid cells and large multinucleated glia cells in the most peripheral portion. There are areas in which the myelin degeneration is but slight, especially at the periph-

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eral part of the area. The glia meshes are distended, but there is no marked change in the density of the neuroglia tissue. Fat granule cells are entirely absent both in the tissue spaces and the vessel wall as shown by the Herxheimer and other stains. The Mallory and toluidin blue preparations show numerous large multinucleated glia cells presenting fibril formation. However, this is not sufficient to cause any marked change in the density of the glia meshes and the process is apparently arrested. The picture is that which is frequently met with after resolution following an edema in disorders of the circulation. We thus have two types of areolar areas: one, the picture of complete resolution without disturbing the original glia meshes; the other, a more advanced process with thickening of the glia meshes and marked myelin degeneration (Plate VIII, Fig. I). Both of these pictures come under the head of secondary changes. The former is an area surrounding one of the branches of a vessel involved in the primary lesion (Plate II, Fig. II), the latter a secondary area of the vessel in which the primary lesion occurs (Plate II, Fig. I). The "areolar zone" of some of the writers is an area surrounding a more rapidly forming sclerosis and which was completed or arrested before the transition zone had reached its terminal stage.

In the brain there are frequently found nonmyelinated devastated areas in the central part of which there appears a small vessel around which are large free spaces surrounded by a wall of dense glia fibrils comparatively free from nuclei. In cross-section the vessels appear torn loose from the surrounding tissue or remain attached by only a few strands of adventitial tissue stretching across the open space. Some of the vessel walls are but little altered, others are almost beyond recognition except for a thin circular strand. Within the space there is a coagulum containing debris, the remains of pigment and fat granule cells. In the lumen of the vessels there are often remnants of the constituent elements of the blood. The lumen of most of the smaller vessels is perfectly clear. Around each vessel the myelia is absent. Both large and small glia cells are proliferating. Sometimes several of these areas coalesce and form larger irregular areas. In the toluidin blue preparations the picture is that of multiple areas of devastation, the result of thrombosis. These perivascular sievelike areas (Plate IX, Fig. III) are probably the result of a circulatory obstruction in the distal branches of the blood vessel in which the primary lesion occurs resulting in a lymph stasis and softening.

SYNOPSIS OF PART II

The various areas described under the second head can be grouped to a large extent as the successive stages of a process which terminates in a secondary sclerosis. Five such stages can be clearly differentiated:

1. Edema and mononuclear cell infiltration.
2. Fat granular cell myelitis.
3. Neuroglia fiber formation.
4. Sclerosis.
5. Retrogression of neuroglia cells, and fat granule cells.

The characteristic microscopic picture presented under low magnification in the toluidin blue and van Gieson preparations shows a demyelinated area having three definite nucleated zones arranged around the lumen of a blood vessel.

The innermost zone involves the vessel wall and the perivascular lymph spaces, and consists mainly of mononuclear epithelioid cells and other mesodermal elements.

The second zone is formed by a cell proliferation in the marginal neuroglia tissue. The cells are large, protoplasmic cells and small neuroglia elements as well as ameboid cells.

The third and most peripheral zone consists of a diffuse neuroglia fiber proliferation in the normal tissue surrounding the perivascular neuroglia zone in which there is an increased number of nuclei and enlarged normal spider cells.

The *first stage* in the development of the secondary sclerotic area is characterized by a swelling of the structural elements and faint staining of a circumscribed area. The nuclei of the vessel wall are increased. There are a great number of nuclei in the perivascular marginal glia tissue and in the peripheral zone the normal spider cells are distinctly enlarged and their nuclei, the protoplasm and their processes show a lighter stain. The myelin and axis cylinders are swollen and faintly stained.

The *second stage* in the process shows large epithelioid cells in the distended meshes of the tissue of the vessel wall and the perivascular lymph spaces. Many of these cells, which are present in large numbers, are fully developed fat granule cells. In the marginal glia tissue there are large multinucleated spider cells with extensive processes. Changes in the peripheral transition zone indicate an exaggeration of all of the elements in a normally retained architecture. The myelin sheaths and axis cylinders are disintegrating.

The *third stage* is the stage of fiber formation in all of the zones. A proliferation of the connective tissue of the vessel wall, marked increase in the fibers of the marginal zone and of the peripheral transition zone with a corresponding myelin sheath and axis cylinder degeneration.

The *fourth stage*, or the stage of sclerosis, is characterized by a dense fiber structure in which the nuclear elements have diminished and the myelin sheaths are no longer in evidence except irregularly

in the peripheral transition zone. The axis cylinders are but few, and those persisting are almost beyond recognition.

The *fifth stage,* or the stage of retrogression, presents a structureless homogeneous demyelinated area. The blood vessel has disintegrated and a homogeneous mass replaces it. The marginal glia zone shows no fiber structure, the fibers have fused into a continuous matrix in which there is seen an occasional nucleus, or a persistent axis cylinder.

The peripheral transition zone shows a dense neuroglia tissue meshwork with few nuclei and a few axis cylinders. The myelin degeneration fades out irregularly and gradually into the normal tissue. The other areas (perivascular sievelike areas, areolar areas and areolar zones) which were described under the second head but could not be placed as definite consecutive stages of the process of secondary sclerosis, will be referred to later.

III. PROCESS OF EVOLUTION

The *process of evolution of neuronic elements* is incident to the evolution of neuroglia elements in the primary lesion of the nerve root.

In three of the cases here cited the ventral and dorsal spinal roots and the intramedullary root-zones and the central gray commissure presented microscopically, nodules differing in structure, and with the various stains, in color, from the foregoing.

Cross-sections of the lower cervical, the upper thoracic and the lumbosacral regions showed a number of such nodules. These nodules are situated in the extramedullary portion of the ventral and the dorsal nerve roots, and extend into the medullary substance of the cord in the region of the root-zones. A number of such nodules are found along the mesial border of the posterior gray horns and within the central gray in the region of the central artery and vein. Nodules of this character were not found in the sections of the brain tissue.

In the van Gieson and Weigert preparation of the spinal cord, the nodules appear to have a close relationship with the pia mater and the blood vessels. They involve especially the pia septa of the posterior columns and the extra medullary pial sheath of the nerve roots (Plate V, Figs. I and II). In the central gray substance they are sharply circumscribed areas with an intervening clear space encircling the nodule, and for but a few fiber strands they are completely isolated from the surrounding tissue (Plate IV, Fig. II—24, and Plate V, Fig. IV). In the pial spaces they form nodules in the vessel wall either on one side or surround the vessel more or less completely. In the white matter they lie free and completely isolated from the nervous elements, though invariably within the adventitia of a vessel.

giving the impression that the connective tissue had secondarily involved the nodule or that the process had arisen from the vessel wall itself. The area around the nodules shows a dense glia fiber proliferation with few nuclei. In the van Gieson preparations under higher magnification, the structure of these nodules presents in longitudinal and transverse cut sections, intertwining fibers containing numerous characteristic nuclei.

The longitudinally cut fibers were stained yellowish-green with a central pink stripe or a deep blue-black center containing a fine pink line which at irregular intervals shows an elongated nucleus in relation to it. The transversely cut fibers have a sharp contour because of the differential stain. The outer zone stains yellowish-green in which there appears a pink ring showing an occasional nucleus. In the center is a deeply stained point which varies somewhat in size and color in the different areas. There are other fibers lying between these which are apparently fine fibrillar connective tissue staining intensely pink and containing elongated nuclei with their long axis sometimes parallel but more often transverse to the fibers. The fibers are densely interlaced and have a whirl arrangement. The nuclei are numerous and of varying types. Those in intimate relation with the nervelike fibers are deeply stained elongated bodies with blurred ends having a distinct network and membrane, but no nucleolus. The long axis of these bodies is parallel to the long axis of the fibers. Some of these appear as broken off at the end; from this broken end, long fibers seem to extend. Other elongated nuclei are not so deeply stained, they are elongated bodies containing a nucleolus. They lie either parallel or transverse in the fine fibrillar connective tissue. Endothelial cells could be distinguished from the other forms by their oval shape, lighter stain, usually containing a nucleolus and their location near the lumen of the blood vessel. In the ramification of the fibers either in the deeper part of the nodule or at the periphery, small fusiform nucleated elements are arranged end to end forming chains apparently in line with the fibers. In the Weigert myelin sheath stain the nodules stain nearly as deep as the surrounding white matter. However, under higher magnification the individual fibers are more faintly stained than the normal fibers and the deeper stain of the nodule as a whole is dependent on a closer opposition of the fibers. In the Bielschowsky preparations the fibers show numerous irregularities and varicose enlargements, here and there delicate twigs are given off which wind around larger fibers and sometimes form into a plexus.

Closely associated with the nodules in the intramedullary portion of the anterior and posterior nerve roots and in the pia mater of the

extramedullary root zone there are areas composed of dense fibrous tissue. Fiber strands appear to extend from this region into the cord and can be traced to the mesial side of the posterior horns and to the base of the anterior horn where they spread out to form a dense area of fibrous tissue. A similar fibrosis occurs in demyelinated portions of the anterior and posterior nerve-roots. These areas consist of a meshwork of finer and coarser fibers among which are small accumulations of lymphocyte-like cells with a deeply stained round nucleus. There are a few other cells somewhat larger than these, that have an oval eccentric nucleus placed to one side in which there is a definite chromatic network. In these fibrous root-zones the van Gieson preparations show a differentiation of the fibers, certain deeply stained pink fibers seem isolated which proved to be axis cylinders in the silver preparations. At the margins of the areas of fibrosis there is a dense neuroglia tissue which fades into the normal tissue by a gradually diminishing density.

SYNOPSIS OF PART III

In the lower cervical, upper thoracic and in the lumbosacral regions of the spinal cord there are fasciculated areas of abnormal fibers and small nodules situated in the outer layer of the pia near the root entry, in the intramedullary root-zones and isolated nodules in the gray and white substance of the cord. All of the areas are intimately connected either with the wall of a blood vessel, with the pial septa of the posterior part of the cord or the anterior fissure.

From the foregoing brief description it is apparent that there are certain abnormal formations which differ from the characteristic lesion of multiple sclerosis but bear a certain relation to the disease, and we can distinguish the following:

1. Isolated nucleated areas in the white and gray substance of the spinal cord which involve the wall of the blood vessel and which consist of embryonic neurofibrils and connective tissue having the arrangement and appearance of a peripheral nerve.

2. Areas of fibrous tissue in the pia mater in which embryonic neurofibers are developing.

3. Isolated areas of fibrosis in the intramedullary root zones and in the anterior and posterior roots.

SUMMARY

The four cases of multiple sclerosis on which this investigation is based were the usual cerebrospinal types; unfortunately in one case the spinal cord was not obtained, but from the distribution of the lesion in the brain extending to the end of the bulb there is no doubt that

also in this case the cord was equally involved. Only one of the cases was personally observed during the progress of the disease. The patient died of acute mastoiditis. Another patient died of pneumonia, one died in a convulsion and one from exhaustion following a number of epileptiform seizures. Their ages were 38, 44, 49 and 54 years. The average duration of the disease in these cases was 10 years. All of the cases showed at necropsy a general adenitis with rather marked glandular enlargement in the bronchi and mesentery. One had a healed tuberculous lesion in the left lung.

The method of examination of the brain and spinal cord of the different cases was uniform and the histologic observations were made in preparations of diffuse and differential stains. The demyelinated areas are of various size and form, though mostly round or oval.

In the *ventral and dorsal spinal nerve roots* the areas are more irregular than elsewhere, though sometimes round or ovoid. Some of the areas have sharp cut margins, others show a gradual transition from the unstained to the normally stained tissue. In the *spinal cord* the areas at the periphery, especially at the ventral and dorsal root-entry, are wedge-shaped. The base of the wedge is subpial, the apex extends into the medullary substance. The areas in the posterior columns are elongated oval shape involving either the posterior median septum or the paramedian septum. Isolated round demyelinated areas occur in the ventral and dorsal horns. These have a very abrupt border. In the central gray substance there are sharply circumscribed round areas more deeply stained than the surrounding myelin sheaths; these areas occur also in the white substance between the posterior horns and in the ventral and dorsal nerve-roots and in the pia in these regions. In the lateral columns, large irregular or wedge-shaped demyelinated areas are present and within these are denser areas usually round or ovoid, only their greater density differentiates them from the surrounding sclerosed tissue.

In the *medulla oblongata, pons, cerebral peduncles, and cerebellum* the areas are round or oval, and the confluent areas are here also apparent. The subpial areas are wedge-shaped with broad base peripheralward. The areas extend into the adjoining tissue in the form of broad isolated processes in which a central vessel can be seen. Such extensions from the periventricular tissue involve the cranial nuclei.

Around the posterior and anterior horns of the lateral ventricles and also in the descending horns of the lateral ventricles the sclerosis assumed the form of long fingerlike extensions from the adjoining white matter. In the medullary rays there are also numerous small, round and oval foci.

In the optic thalamus, the caudate and lenticular nucleus, the areas are frequently round, very numerous and small, though sometimes confluent. Within the confluent areas small, round denser areas are apparent which indicate the original foci. Symmetrical involvement of the basal ganglia is strikingly evident.

The internal capsule, the external capsule and claustrum, also the convolutions of the island of Reil show quite round, isolated areas of varying size and a striking symmetry of the two sides. The sieve-like areas around the branches of the lenticulo-striate and strio-thalamic vessels are marked and constant in all of the cases.

It appears that not only these areas, but all of the demyelinated areas occur within the radius of a blood vessel as far as that territory can be determined. The primary sclerosed area is invariably within the vessel zone.

In the cerebral cortex the demyelinated areas are more variable in size and shape than elsewhere. Some of the areas appear as extensions from the white matter into the gray. The shape of these extensions seems to conform to the radiations of the nerve-fibers and appear as elongated sometimes curved or pointed areas. Numerous round or ovoid areas can be made out entirely within the cortex. They may be situated in the tangential layer or in the supraradial or intraradial network. In some of the areas a central vessel was apparent, in others numerous capillary vessels in various positions are seen within them.

Some of the areas appear to spread from the surface inward. Such areas extending from the surface into the convolution are often wedge-shaped, sometimes in the form of an irregularly curved process with its convexity to the surface. The outline of these areas is well defined. Some of them extend as far as the subcortical white matter.

Confluent areas with complete demyelination of a whole convolution and sometimes extending around a sulcus to another convolution was observed.

In the cerebellum, the medullary core is uniformly involved in all of the cases. The demyelinated areas are small, mostly round; the larger ones consist of several confluent areas. The cortex shares in this involvement. Small, round areas are found in almost every section of the cerebellar cortex. None of the areas appear to extend from the cortex to the medullary core, or vice versa. A remarkable symmetry in the cortical areas is also here indicated.

From the foregoing it is apparent that the demyelinated areas are distributed over the entire central nervous system, that they are round or oval, or modifications of these forms when they originate in the medullary substance, cortex or gray substance of the cord, while the subpial areas and the areas in the pial septa are wedge-shaped. In the confluent areas the original round or ovoid focus can be differentiated.

TYPES OF DEMYELINATED AREAS IN THE WEIGERT-PAL AND KULSCHITZKY PREPARATIONS

From the standpoint of demyelination there are *three definite types of areas.* However, a fourth type is apparent because of a more intense myelin sheath stain than in the normal tissue.

1. (Plate IV; Plate V, Fig. II; Plate VIII, Fig. IV). The limits of such an area is abrupt, and there is no gradual restoration of the normal color in the tissue surrounding it. In the area itself the medullary sheaths have entirely perished, and there is no evidence of the products of degeneration. From the earliest period of development the processes of new formation, disintegration of the myelin sheaths and retrogression of cellular elements are relatively proportionate. The characteristic demyelinization of this type is that the myelin sheaths appear thinner but definitely stained. In longitudinal section one observes a number of very fine granules and some larger spherical bodies which are attached to the outer well stained border of the myelin sheath, and as these break away and disappear others are formed until the myelin gradually becomes thinner, and finally a series of these bodies represents the remnant of the myelin sheath which undergoes the same process.

2. (Plate I, Fig. IV and Plate XII, Fig. I). Here the demyelinization presents itself in various forms. Early in the process the area is diffusely stained and appears edematous, the whole ring of myelin is broken up into smaller and larger globules with smaller intervening granules. In longitudinal section, there are exaggerated varicosities of the fibers and the whole fiber is broken up into large oval vesicles; some of these are found in the more central part of the area where the demyelinization is well advanced. The peripheral zone shows an irregular disintegration of the myelin sheath in the same manner. There are many badly stained fibers and the limits of such an area depend on a gradual and irregular restoration of the normal stain of the myelin sheaths. The process of new formation does not keep pace with the process of disintegration in the areas of this type.

3. (Plate VIII, Fig. I). Such areas are more or less tumefied. The whole area is diffusely stained, the individual fibers are not well stained and the myelin degeneration occurs simultaneously in the whole area. The myelin sheath is rapidly broken up into variable segments. These areas are not sharply defined, and under higher magnification show a gradual increasing intensity of the normal myelin sheath stain toward the periphery. The process completed shows a demyelinated area containing small irregular empty spaces with thickened septa; occasionally there are larger spaces within them which appear to be

the result of a confluence of several of the smaller spaces indicated by the projecting broken ends of the dividing tissue.

4. (Plate VII, Fig. IV—43). There are well defined areas in the spinal cord and nerve-roots because of a deeper staining. However, under higher magnification it is shown that this is dependent on the greater density of the myelinated fibers. The individual fibers are not so deeply stained as the normal fibers in the surrounding tissue. The areas are sharply circumscribed, consisting of elongated irregularly coursing fibers with connecting bridges forming a reticulum in the wall of a blood vessel, the lumen of which is distinguished in the center or toward the periphery of the area. Some of the fibers stain more deeply than others, and all of them, while variable in size, are finer than the fibers in the normal tissue. The tissue surrounding these areas shows a contrast to the normal tissue by its paler staining.

BIELSCHOWSKY AXIS CYLINDER PREPARATIONS

The *Bielschowsky axis cylinder* preparations present histologic variations in the three types of demyelinated areas which are in accord with the process of disintegration of the myelin sheaths in the respective areas. In the fourth type they present no degenerative changes, but not any of the axis cylinders are fully developed normal nerve-fibrils.

1. (Plate IX, Fig. II; Plate IV, Fig. IV.—42). Maintaining the classification adopted in describing the myelin sheath preparations, the area of this type is striking for the comparative persistence of the axis cylinders. While this persistence is only a relative one the changes which lead to the destruction of the axis cylinders in this type are sufficiently characteristic to differentiate them from alterations in other types. In cross-section the remaining axis cylinders appear more prominent than in other areas because of a greater contrast in the color than in the normal tissue. Most of them are larger though some are smaller, they are fewer in number, and while not so well stained the surrounding tissue is nearly colorless. Around each fiber a single or double circle can be distinguished; this is dependent on color contrast as no difference in structure can be seen. There is little change in the position and form of the axis cylinders in the cross-section of the areas of this type at various periods of development. They become more apparent as the areas advance in development by reason of color contrast; the staining qualities of the tissue surrounding the axis cylinders within the area diminish while the axis cylinders themselves appear more dense.

In longitudinal section more definite changes are recognized. In the course of the nerve-fibers there are spindle-shaped enlargements

of various size. They are homogeneous, dense, fairly well stained elements which change little in color with the advancement of the sclerosis, but the variations in size become more apparent, the former narrow spaces separating the axis cylinders from other structures become obliterated by proliferating wavy glia fibrils forming a dense sheath around the persistent nerve-fibrils. The longer axis cylinders can be traced from the sclerotic area into the normal tissue. The change in color is abrupt at the peripheral margin of the demyelinated area and after passing through a narrow transition zone the normal myelinated axis cylinders appear. In the transition zone the nerve-fibers show a slight change in color but no perceptible change in structure, though the variation in size and the irregularity in outline is striking when compared with the normal fibers in the surrounding tissue. There are no demyelinated axis cylinders in the transition zone of this type of demyelinated area.

2. (Plate IX, Fig. I—42). The area belonging to the second class present changes in the axis cylinders which correspond to the degenerative changes following demyelination in other conditions. The earliest observation is a homogeneous swelling which appears in the area as a whole; the axis cylinders become more or less attenuated. The variations in size are striking, very few approach that of normal fibers. In longitudinal section the qualitative changes affect the largest number of fibers and at some time all of the fibers, as there are no persistent axis cylinders in this type, in the sense of that of the primary sclerotic areas.

After the axis cylinders become swollen, they become shrunken irregularly and there appear spindlelike enlargements. These, as well as the thinner parts, become segmented and disintegrate into homogeneous clumps and fine irregular granules.

From the variations in the color it is apparent that there are qualitative differences in them, and some of them persist as isolated bodies and appear in cross-section as irregular dark stained bodies which are with difficulty differentiated from the persistent axis cylinders of the demyelinated area Type I, though they are granular, irregular, more deeply stained, and there are usually secondary granules situated in the same space with the larger ones. In longitudinal section, the appearance of the fibers in the different zones varies apparently only in degree. Isolated axis cylinders can be traced through the sclerotic tissue, and transition zone into the normal tissue. They are swollen and tortuous, in the apparently normal tissue they are easily distinguished, among the normally myelinated fibers they appear as tortuous faintly stained shrunken demyelinated fibrils as far as they can be traced.

3. (Plate IX, Fig. IV). The area of the third variety shows no trace of the original axis cylinders. There are, now and then, irregular deeply stained granules lying in open spaces which may or may not be parts of degenerated axis cylinders. In the sclerosed zone surrounding these areas no axis cylinders could be traced, but color difference in the transition zone appears to be dependent on certain demyelinated deeply stained axis cylinders, which can be traced into the normal tissue as changed myelinated fibers.

4. (Plate VIII, Fig. IV—45). This type appears as deeply stained sharply circumscribed, mostly round masses of fibers. The fibers stain intensely dark and show numerous irregularities and fine varicosities. From the thicker fibers there extend fine branches which frequently end in bulbs. Some of the fine twigs appear to entwine the larger fibers, others form plexuses within the vessel wall where they eventually form a dense interlacing and whirl arrangement.

OTHER PREPARATIONS

The *Mallory phosphotungstic acid hematoxylin and Weigert neuroglia stain* and Alsheimer and van Gieson preparations present changes in the neuroglia tissue which are essentially different in the various types of areas.

1. (Plate VII, Figs. I, II and III.) In the first type the early microscopic picture shows numerous large neuroglia elements in the transformation into glia fibrils and glia nuclei, which in their further evolution form dense concentrically arranged bundles of undulating neuroglia fibers between which there is a dense reticulum of finer fibers with few nuclei. Surrounding these areas there is a neuroglia fiber proliferation with retention of the normal neuroglia architecture. The neuroglia reticulum becomes more dense, the intervening spaces narrower and some of them are obliterated by a fine neuroglia reticulum.

2. (Plate I, Figs. IV and V; Plate VIII, Fig. II.) The second type can be differentiated into three zones. The perivascular and peripheral zones present a dense fiber reticulum with no definite intervening spaces. The fibers are of varying size forming trabeculae which interlace with one another and a reticulum of finer fibrils lying between them which eventually form a dense homogeneous matrix. The innermost zone presents rows of fiber-forming nucleated elements in the adventitia. The fibers have no definite arrangement, but form a dense felt-work. The peripheral zone presents the architecture of normal neuroglia tissue with an increase in the nucleated elements. The neuroglia trabeculae increase in density and a dense neuroglia

reticulum of finer fibers is formed between them. This zone eventually becomes fused with the inner zone.

The transition zone shows an increase in the nuclear elements and an increase in the neuroglia fibers without distorting the normal architecture.

3. (Plate IX, Fig. III.) The third type shows no neuroglia tissue within the area, but the neuroglia tissue surrounding the area shows that the normal architecture is retained, and there is a great density of the fibers and a larger number of nucleated elements. In the brain there are areas (perivascular sievelike areas) containing large open spaces into which project (in longitudinal section) blood vessels or a large space around the vessels (in cross-section) is shown. The spaces within the area are surrounded by a dense wall of neuroglia fibers. The constituent elements of the vessel wall are separated, this forming elongated spaces in which are found the remains of cellular elements.

4 and 5. (Plate II, Fig. II, and Plate VIII, Fig. I.) The fourth and fifth type ("areolar areas and areolar zones") show a single irregular clear space or a number of clear spaces, some of which are confluent. These areas are surrounded by a dense wall of neuroglia tissue, the result of a compensatory reaction in the neuroglia dependent on the destruction of the tissue within the area ("areolar area"). In another but similar type ("areolar zone") the normal architecture of the neuroglia tissue surrounding such areas can be recognized, but the fibers of the trabeculae are more compact.

ANOTHER PREPARATION WHICH SHOWS WIDE VARIATIONS

The *toluidin blue preparations* show a wide variation in the cellular elements of the different types of sclerotic areas. The mesodermal and ectodermal elements are readily classified not only by their structure which is so beautifully brought out, but also by the difference in color.

1. (Plates V, VI and X.) In the actual primary sclerotic area the ectodermal elements predominate; in fact, very few pathologic mesodermal elements enter the primary plaque formation. In the earliest areas there are a large number of large round or slightly oval cells which lie in the adventitial tissue partially or completely surrounding the lumen of a vessel in a single or double layer. The cell protoplasm is colorless and structureless, but sharply circumscribed, in the center of which is a deeply stained grayish-purple to deep blue nucleus with a distinct nuclear wall in which no definite structure can be made out at this time. In their further evolution, as is shown in other areas, they are transformed into various types (17, 34, 8) which can be followed in the evolution of the primary sclerotic area from their first development to the last stage of retrogression (43).

A progressive enlargement of the nuclei is the first change apparent. The chromatic structure of the nucleus becomes differentiated and more or less definitely arranged; at this period the protoplasm around the nucleus becomes deeply stained, which finally extends to all of the cell protoplasm. In many of these large cells there are mitotic figures, others have two or more nuclei and the cell protoplas shows lines of division. Now there are irregularly triangular cells (34) developing large protoplasmic processes (8) in the margins of which the protoplasm becomes differentiated into fine striae (8) (as is shown in the van Gieson preparations). In other cells the fibril formation is evident in the presence of recurving fibers with the convexity in close proximity with the nucleus (8). The regressive changes in the glia cells are indicated by the various forms of large faintly stained nuclei with little or no protoplasm around them, and finally the large, round, granular bodies showing a dissolution of the nucleus itself, which is also evident in the absence of the nucleated elements in well formed primary sclerotic areas. Around the sclerotic area of this type there are large, irregular, protoplasmic processes extending in all directions; the cytoplasm of the process is faintly stained, their margins are indistinct. The nucleus is large, round or ovoid, well stained with few irregularly distributed chromatic bodies of variable size. These cells are apparently ameboid neuroglia cells which lie in close proximity to the marginal tissue. There are other small nucleated elements which are like the small nucleated elements of the normal neuroglia tissue except that the nuclei are somewhat larger and more deeply stained. Besides these there are numerous spider cells more or less regularly arranged around the sclerotic area.

2. (Plate I, Figs. I, II and III.) The three nucleated zones and the variegated color picture in each makes a striking contrast between the area of this type and the foregoing. The predominance of the mesodermal elements in the secondary sclerotic areas is evident from the very beginning of this process.

In the perivascular zone the largest number of cells are round or irregular ovoid vacuolated bodies of considerable size with a large, round, central or peripheral deep blue nucleus more often situated at the narrowest point in the periphery (9). The cell protoplasm contains deeply stained, blue granules and lumps of variable size and shape. Many show more or less light brown pigment. Some of them are completely filled with this, the nucleus is stained blue and is of uniform chromatic structure. Some of these cells are packed with large irregular granules so that only the nucleus can be recognized. These cells are present in great numbers and lie in spaces between the tissue trabeculae of the media and adventitia. A smaller number of these cells appear in the peripheral nucleated zone where they are

separated from one another by the protoplasmic processes of the enlarged multinucleated neuroglia cells.

The protoplasm of the neuroglia cells takes on a faint purple uniform stain and appears as a homogeneous mass in which there are more or less centrally situated, deeply stained, round, or slightly ovoid nuclei. In some of the cells the cytoplasm is but faintly stained; in these a definite reticulum can be seen which takes on a light purple color; variations in form of the cell body and nucleus can be readily traced as transitions from the newly formed mesodermal elements to the fully developed fat-granule cell. In the same zone there are large irregular multinucleated cell bodies with long protoplasmic processes. The nuclei of these cells stain well, but a lighter blue than the former. They contain numerous small deeply stained granules of uniform distribution. The cell bodies stain faintly or not at all. The cytoplasm is finely granular though a few coarse granules occur in the cellular substance. Variations in these cells and nuclear changes which indicate a mitosis and changes in the protoplasmic processes present fiber formation from the earliest differentiation to complete transformation into neuroglia fibers (van Gieson stain).

The intima of the smaller vessels shows a nuclear increase. There are elongated oval cells showing nuclear and cell division in various stages. The nuclei stain a light blue with a deeply stained purple nucleolus and deep blue chromatic bodies. The cytoplasm stains a pale blue and appears finely granular. Some of the nuclei lie perpendicular and oblique to the vessel wall giving the impression of a migration into the tissue. In the adventitia, aside from the elements already described there are numerous well stained, elongated nuclei, most of which are placed parallel to the adventitial fibers. The nuclei take on a deep blue stain with a nucleolus of a deeper blue color.

In the adventitial spaces there are other types of cells, some of them are almost square with round or ovoid nuclei showing a radial arrangement of the chromatin and more or less deeply stained centralized purple cytoplasm. Other cells, somewhat smaller, are round or slightly ovoid with a comparatively large deeply stained, blue nucleus placed in the center or periphery of a mass of finely granular pink or purple cytoplasm. Irregularly scattered among the other cells are numerous small, well stained nuclei of a light blue color with deep blue chromatic bodies, some of which show a regular radial arrangement; in others, the chromatic bodies are few and not definitely placed.

The peripheral nucleated zone shows principally two types of cells. The largest number are large protoplasmic bodies. They are but faintly stained and take on a pale purple color or a very slight reddish tinge. The cell bodies of some of these elements are apparent only because of a faint, light purple margin which outlines the form of the

cell, the central cytoplasm being colorless. These cells are arranged in rows of one or two layers but frequently separated from one another by somewhat smaller nucleated elements of the enlarged spider cell type. They stand out prominently though fewer in number; they are deeply stained, and for this reason show a striking contrast under low magnification.

In the outermost nucleated zone or the transition zone there are numerous small nuclei among which are irregularly scattered larger elements. The size of the large cells varies, so does their form; some of them are round or irregularly oval. The cytoplasm has a faint purple color, in some there is no stain perceptible, and it is a grayish margin that outlines the cell body. Numerous fine granules are seen uniformly distributed throughout the cell. The nucleus is large, round or oval, sometimes half as large as the cell and takes on a blue color which varies from a deep blue to the most delicate tint. Within the nucleus there are well stained, fine, blue granules. The distribution of the chromatic substance is variable; in the smaller nuclei it appears quite uniform throughout the nucleus, and in the larger nuclei the granules are found only in the periphery—occasionally there are two or three nuclei in this type of cell.

In the same zone there are other large, round, deep blue nuclei situated in the center or slightly to one side of an extensive mass of branching cytoplasm which stains a light purple color. Still other smaller deeply stained nuclei show little or no protoplasm surrounding them, but these are apparently surrounded by numerous finer or coarser fibers (neuroglia-fiber stain).

The cellular elements of the "areolar areas" are mainly of two types which are separated into two zones. Within the distended network of the neuroglia tissue there are large, round or ovoid cells with a large, central or peripheral nucleus which is somewhat variable in its finer structure and staining. Some of the nuclei stain deep blue in which no definite chromatic structure can be made out; other nuclei show a light blue background with deeply stained and regularly placed blue granules. A number of the cells of this type have two and three nuclei. The cytoplasm has a definite reticulum, and in many of the cells there are large vacuoles and a large amount of light brown, stained substance—this sometimes fills the entire cell. These same elements are numerous in the adventitial spaces of the dilated vessels in the periphery of these areas. Here one observes a large number of small, round, mononuclear cells. The nuclei of these cells are deeply stained with a definite chromatic structure which stands out well because of its deeper stain.

The peripheral zone of these areas contains numerous nuclei of variable size and structure. The small, round, deeply stained nuclei

predominate; surrounding these there is but a small amount of cytoplasm; sometimes this is indicated by a delicate gray ring around the nucleus with an unstained, narrow space between it and the nucleus. However, it is shown in the preparations stained for neuroglia fibers that these nuclei are the centers of radiating fibers. The large nuclei lie in the center or periphery of a large, irregularly branched mass of protoplasm which takes on a faint purple stain; in some of these cells there are two or more nuclei and other irregular well stained bodies and here and there light brown masses. There are numerous small nuclei quite regularly distributed throughout the meshwork and situated at the nodal points of the network—around these no cytoplasm is apparent.

The "areolar zones" have a smaller number of nuclei and present a more regular distribution, situated at the nodal points of a dense network. They are largely of the smaller type and are deeply stained; the nuclei show a nuclear membrane. In the dilated meshes there are, here and there, large, round or ovoid cells with a central or peripheral nucleus of a light blue color. The cell body has a faint purple color showing a reticular structure; in some of the spaces there are irregular bodies which appear to be parts of cells of this type.

The "perivascular sievelike areas" present but few nuclei in the dense wall surrounding these open spaces. There are small, round, deeply stained nuclei with a well differentiated nuclear membrane but there is little or no cytoplasm surrounding them. In the spaces between the constituent elements of the vessel wall there are a few large, round or ovoid, nucleated elements and more or less coagulum in which there are numerous granules of light brown pigment and the remains of degenerated cells.

FURTHER CLASSIFICATION

The *Herxheimer Scharlach R.* preparations permit of a classification of the different types of areas as well as of a differentiation of stages in the development of certain areas.

1. The *areas of the first type,* or the primary sclerotic plaques, are strikingly free from red stain. The nuclei of the various types of cells are well stained by the hematoxylin counter stain, the cytoplasm of the various elements in the perivascular zone shows no red stain. In the transition zone one can distinguish a few large, irregular cells which contain fine granules that are stained bright red. There is no red stain outside of these cells.

2. The *sclerotic areas of the second type* stand out prominently. They appear under low magnification as red points throughout the microscopic field among which are irregularly scattered sharply circumscribed colorless areas. Under higher magnification it is shown

that in the three zones of these areas there are large, round or ovoid cells with large, well stained central or peripheral nuclei surrounded by a mass of bright red, densely packed clumps and fine granules. These cells are more dense in the perivascular zone, but are numerous in the peripheral zone and also in the transition zone. This type of cell is present in all of the stages of development of this type of sclerosis. The number of cells diminish from the periphery as the processes advance.

3. *In the third type of areas* in the spinal cord and in the root-zones and extramedullary roots, the red stain is entirely absent and the areas are stained deep blue because of the presence of a large number of nuclei.

The other types of areas (the areolar areas, areolar zones and sievelike areas) all have more or less red staining. The stain is largely within the large, round or ovoid cells, though there are loose, red granules in the spaces of the areolar areas. The red stained cells are more numerous in the areolar zones and in the tissue surrounding the sievelike areas.

It is opportune at this point to compare the preparations of Alzheimer's method A and C with the Herxheimer preparations. In the former, especially in the sections treated according to the method C the areas of the first type (primary lesion) present in the perivascular zone, large, irregular cells with broad protoplasmic processes. The cell protoplasm is stained green in which there are a few variable granules stained bright red. There are no red granules outside of these cells. In the peripheral reaction zone this type of cell is present in larger numbers, and the red stained granules within the green cell body are numerous. There are no other cells containing these red stained granules, and the red granules are not seen outside of the cell body.

In the second type of the sclerotic areas (secondary lesion) there appears an interesting color differentiation. In the large, round or ovoid cells so numerous in this type of area, the granules are stained a brownish-red while the granules in the large, branched protoplasmic cells are stained a bright red. The granules in the former are more regular and more dense, while the latter are fine irregularly scattered particles. The large, round or ovoid cells are densely packed around the vessel lumen. The large, branched, protoplasmic cells are found in the peripheral zones. In the other secondary types of areas similar observations are made. In the third type where neither the large, round or ovoid cells of the foregoing variety occur, there are no red stained granules.

CONCLUSION

Considering the observations in the foregoing pages and the descriptions and illustrations of other writers in which there is really no marked discrepancy except in the conclusions, it is a fair deduction to say that the various lesions in multiple sclerosis cannot be placed as successive stages in a process as a whole, which forms the characteristic sclerotic plaque. On the other hand, and on the same basis, it is possible to differentiate a series of pathologic changes which are embryologically the successive stages of three distinct processes.

Cytologically, there are three well defined types of lesions the result of one common etiology.

The first or primary lesion consists of elements derived from the ectoderm. There are embryonic cells in all stages of development in the process of neuroglia fiber formation and subsequently presenting the various steps of retrogression. The cell elements are:

1. Undifferentiated ectodermal cells.
2. Neuroglia cells showing mitosis.
3. Fiber-forming neuroglia cells.
4. Multinucleated neuroglia cells.
5. Ameboid neuroglia cells.
6. Neuroglia cells showing retrogressive changes.

The second type of lesion consists of:

I. Mesodermal elements in all stages of proliferation incident to an exudate and a destruction of the medullary substance as follows:

1. Fat granule cells and endothelioid cells of various types showing developmental and retrogressive changes.
2. Fibroblasts.
3. Lymphocytes.
4. Mononuclear and polynuclear leukocytes.
5. Plasma cells.
6. Mast cells.

II. Ectodermal elements in all stages of development in the process of neuroglia fiber formation reactionary to a biogenetic imbalance. These are:

1. Multinucleated neuroglia cells.
2. Large ameboid neuroglia cells.
3. Large protoplasmic glia cells showing steps incident to fiber formation.
4. Ectodermal cell types indicating retrogressive changes.

The third lesion consists of ectodermal elements resembling the cells of the sheath of Schwann and modifications of such types and spindle-shaped cells.

1. Undifferentiated cells.

2. Fusiform cells with blurred ends and elongated nuclei (neuroblasts).

3. Square cells with a large, round, central nucleus.

4. Elongated, club-shaped elements with long, tapering ends showing a splitting up into fine fibrils.

The changes in the nerve cells in the different areas cannot be so definitely isolated for the various lesions, but the degree of destruction and the rapidity of the process leaves certain characteristic feaures in the different types of areas. Binucleated ganglion cells were demonstrated in the cerebral cortex of all the cases.

In the vicinity of the primary lesion many of the ganglion cells were altered in character. The changes in the cells varied from an absence of chromatic substance in the periphery of the cell to a complete centralization with displacement of the nucleus and all stages of atrophy of the cells.

The nerve cell changes in the secondary areas present, on the whole, a different picture. The majority of the cells have lost their natural contour, the pyramidal cells are now ovoid and bulging, they are diffusely stained and there is a complete dissolution of the granules. Some of the cells are vacuolated, the nucleus is eccentric and all stages of cell atrophy are represented.

In the areas of the third type the changes in the ganglion cells are identical with those of the first type, but the alterations are not so marked. To a remarkable extent the ganglion cells are preserved in the vicinity of the areas in the gray matter of the cord. Though many cells are altered the majority are in apparently normal condition.

GENERAL CONSIDERATIONS

I. The first type, or the primary characteristic lesion *per se*, is of ectodermal origin and no other elements are originally a part of the formation of this type of sclerotic plaque. The whole process can be traced step by step from an undifferentiated cell through the different stages of cell proliferation by mitoschisis. The type of cell considered as the primary element can be demonstrated only in the areas of this type. They are invariably lodged in the adventitia and it is in this tissue that later the fiber proliferating cells are present in large numbers. The close relationship between the undifferentiated elements and the fiber-forming cells is evident in the character of the

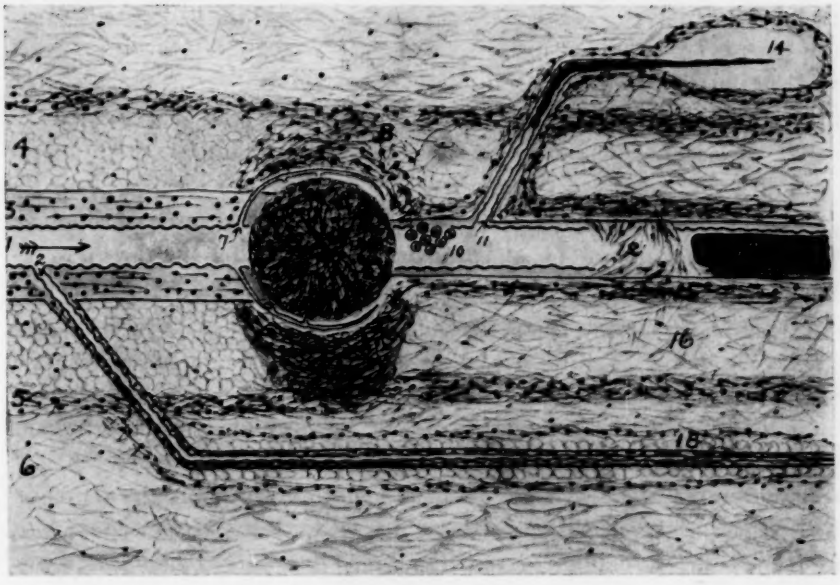


Fig. 1.—The illustration shows the relation of the primary lesion and the secondary changes in the cerebral cortex. The figure represents a blood vessel in which the primary lesion is located at (9). This consists of a mass of interwoven neuroglia fibers among which are scattered numerous neuroglia nuclei, and a section through it in any plane shows the same compact structure. It has developed from undifferentiated cells within the vessel wall. Its slow growth has gradually obliterated the lumen and the vessel wall causing secondary changes both in the proximate and distal portion of the vessel and its branches. About the tumor is a secondary neuroglia proliferation of fibers and nuclei (8). The network is less dense than that of the tumor and the arrangement of the fibers resembles that of the normal architecture. The new-formed neuroglia growth is nourished by the newly formed capillaries (7). Proximal to the primary lesion the blood vessel wall is edematous and infiltrated with small round cells, fat-granule cells, plasma cells, mast cells and transitional cells (3, perivascular zone). The tissue surrounding this zone shows a loose meshwork with wide spaces which may contain fat-granule cells and large protoplasmic neuroglia cells or many of the spaces are empty with but a remnant of an axis cylinder (4, peripheral nucleated zone). Bordering this, the neuroglia tissue shows an increased number of nuclei and the neuroglia trabeculae are thickened, the normal architecture is retained (5, transition zone). More peripheralward there is a gradual change into the normal tissue (6). A branch given off (2) proximal to the primary lesion will show the same changes, and if the branch extends some distance beyond the primary lesion these changes might occur in close proximity to the primary lesion in a cross-section at this point (18).

The distal portion of the blood vessel is obstructed. There are changes in all of the coats of the vessel wall especially the intima. A white thrombus (10) may form. The vessel may be obliterated by a thrombus (17), and proximal to this a secondary sclerosis may occur (12) which completely obliterates the vessel wall and lumen. The reaction about the blood vessel depends on the rapidity with which the vessel is occluded. Distal to the primary lesion there are two nucleated zones (15 and 5) which may be separated by a zone comparatively free from nucleated elements (16). A similar zone is seen in the tissue surrounding the proximal portion of the vessel; in this there are wide meshes and few nuclei with remnants of axis cylinders (4, "areolar (11) zone"). A terminal capillary or precapillary branch given off from the distal portion of the vessel may become blocked by a thrombus and a perivascular softening occurs with a secondary neuroglia reaction forming a dense wall about it (14, "sievelike areas").

protoplasm after cell division. In these newly formed elements, the toluidin blue stain brings out well stained, regularly placed, perinuclear granules. As the cells enlarge these granules move toward the periphery and now, light, strongly refractive lines become visible, and in the silver preparations are shown to consist of fibrils which are continuous with the striations in the protoplasmic processes of the cells. These become differentiated into fiber bundles which merge with the surrounding meshwork of similar fibers. At this point the process is limited to the vessel wall apparently extending throughout the adventitial tissue in all directions and finally surrounding the lumen as it extends to the other coats from the syncytial chain of neuroblasts which consist of fiber-forming elements in different stages of development. The difference in structure and arrangement of the newly formed tissue, clearly separates it from the surrounding tissue. Newly formed capillaries which extend into the area mark this point of separation. As the obliteration of the vessel proceeds, the surrounded nerve fibers become demyelinated and the neuroglia increases in density. The central process extends toward the periphery and infiltrates the normal neuroglia reticulum until this is obliterated and a dense homogeneous matrix is formed in which there are persistent axis cylinders. The limits of the area and the resulting secondary changes are determined by the natural conditions of the location in which it develops, that is, the structure of the tissue, the size of the vessel, its course, and whether the main stem, a smaller or a larger branch, or a terminal twig, is the site of development. The abrupt margin of the area is dependent on the limitation of the tissue in which the embryonic neuroglia cell develops. The cells do not migrate in the medullary substance and the extension of the process to the medullary substance is a fibrous penetration and a secondary proliferation of the neuroglia tissue. This is evident in the merging of the newly formed fiber bundles of protoplasmic processes with the fiber meshwork of the surrounding tissue. The primary lesion, therefore, is a new growth which has its origin in an indifferentiated embryonic cell lodged in the adventitia of a blood vessel which, under certain conditions, develops into a neuroglia fibrous tumor mass which in its course of development destroys the vessel wall and finally obliterates its lumen; at the same time new capillaries are formed in the margin of the new growth which extend into the mass of newly formed fibers. As a result of this, certain secondary changes occur. In the tissue surrounding the primary lesion there is a reaction consisting of an increased number of nucleated elements and a thickening of the normal neuroglia fiber structure.

II. The second type, or secondary lesions of multiple sclerosis, are the direct result of the gradual obliteration of a blood vessel and consist of several forms:

1. The secondary sclerotic plaque of the three zone type is formed in the distal part of the same vessel in which the primary lesion occurs. Frequently the vessel is thrombosed which is shown in cross-section. Here there is a proliferation of the cells of the adventitia and intima with the formation of new connective tissue and a perivascular proliferation of the neuroglia nuclei and fibers. The neuroglia fibers extend into the adventitia and fiber-forming neuroglia cells are here demonstrated. The connective tissue and the neuroglia fibers are shown to be interwoven. The vessel walls become gradually a dense homogeneous ring and are often obliterated by the overgrowth of neuroglia fibers forming a homogeneous matrix in which there are but a few or no persistent axis cylinders. In the process of formation there is a "fat granule cell myelitis," demyelination takes place more rapidly than in the primary lesion, and a marked compensatory neuroglia reaction occurs forming a dense network which eventually is replaced by the secondary sclerotic plaque. If the process is arrested before the perivascular neuroglia zone and the transition zone have become fused by the proliferation of the neuroglia there remain a reticulum between the two zones in the spaces of which are displaced swollen axis cylinders and portions of cells the result of degeneration. This intervening space is spoken of as the "areolar zone."

2. The "sievelike areas" are the result of small areas of softening following a thrombosis of a terminal distal branch of the vessel in which the primary lesion has occurred. Those areas are surrounded by a dense wall of neuroglia tissue, the natural result of a reaction in the neuroglia tissue. In the space thus formed there is a blood vessel or parts of the wall of a blood vessel and sometimes cellular elements and particles of tissue.

3. On the proximal side of the new growth the vessel becomes dilated and an exudate into the vessel wall and the surrounding tissue takes place. The adventitial spaces are widened and the glia meshes distended. There are wide spaces in the media. In the earlier stages of this process there are a large number of fat granule cells and a rapid destruction of the vessel wall, and the myelin in the surrounding tissue disintegrates. All the cellular elements which are ordinarily present in lesions of this type are here observed. Other areas of this type show no cellular elements the results of the exudate, and all of the spaces are empty with the exception of remnants of tissue here and there. A slight thickening of the glia trabeculae and large multinucleated glia cells in the process of fiber formation is the characteristic

microscopic picture of the "areolar areas." The latter is, in part, the result of resolution of the former infiltrated area and, in part, the result of the process of preparation. The same lesion may occur in the branches given off on the proximal side of the primary lesion.

III. It is sufficiently evident from the detailed description of the patches composed of interlacaing nucleated fibers and fusiform nucleated elements that these are tumors consisting of embryonic neuronic elements.

The fact that these well-isolated nodules do not stain in the neuroglia preparations and that they appear as dark areas in the silver preparations in contrast to the characteristic light patches, differentiates them from the lesions of multiple sclerosis. The well-formed nodules are identical with the neuromas of the central nervous system. These are observed only in the spinal cord and on the nerve roots. The lymphocyte-like cells and the square cells forming definite rings around the earlier areas of this type are identical with the cells of the sheath of Schwann and the areas of this type occurring in the nerve roots are of the same structure as those in the central gray matter of the spinal cord. The type of cell, its characteristic nucleus and general morphologic structure which forms the principal element in these nodules and the syncytial neuroblast chains consisting of fibers with interstitial nuclei showing a naked axis cylinder and therefore a nerve fiber in the process of development, gives sufficient proof that these nodules are neuromas. The nodules in the extramedullary nerve roots are identical with those situated within the connective tissue septa in the spinal cord and within the connective tissue layer of the blood vessels of the central gray matter.

The undifferentiated cells (lymphocyte-like cells) occur as such in the neuromas in the primary lesion of multiple sclerosis, in syringomyelia and very similar cells in the gliomas. In syringomyelia there are in addition to the central gliosis, gliomas as well as neuromas, and direct connection can be traced between fibers of the entering posterior roots and the fibers infiltrating the intramedullary root zones. The same condition exists in multiple sclerosis, as has already been related.

The occurrence of neuromas in the nerve roots and in the spinal cord in multiple sclerosis is not an unusual incident, as both types of lesions are illustrated by other investigators though not recognized as different types of embryonic tissue, but regarded as stages in the formation of the sclerotic plaque. It is not possible to differentiate these until the cells of the syncytial chains have become fiber-forming elements, or later when this process is well advanced. The presence of neuromas in multiple sclerosis is not an accidental occurrence, but from the evidence available the origin of the primary lesion of mul-

tiple sclerosis and the neuromas is traced to the same developmental disturbance. Both forms are found in the nerve roots with chains of cells identical in both. Tumors of the same structure as those in the nerve roots occur in the spinal cord, both develop primarily in the adventitial tissue and the same cell chains are in evidence in both types. When we consider that the embryonal neurocytes are capable of differentiating to form ganglion cells, glia cells and nerve fibers and probably the nerve-fiber cells (cells of Schwann's sheath) and neuroglia-fiber cells are derived from the same mother-cell, it is readily understood how this combination is not only possible but probable. Both the neuromas of the central nervous system and the primary lesion of multiple sclerosis are derived from residues of neuroblastic tissue which becomes dislodged from the naturally developing embryonic layer of the nervous tissue, and is distributed to the various foci of development by the loose areolar tissue covering the sheaths of nerves, the epidermal tissue and the adventitial elements of the vessels of the spinal cord septa and of the pia-trabeculae of the brain.

The separated cells continue to develop in a fairly normal way to a certain point. This undifferentiated tissue remains dormant until certain pathologic conditions (hyperemia, inflammation, trauma, exposure, etc.) which disturb the biogenetic balance of the tissue, then these cells become differentiated into the various types of new formation in which the neuroblastic tissue attains full maturity, forming fully developed nerve fibers and neuroglia fibers. If the neuroblastic tissue does not develop normally some focus of undifferentiated tissues may become malignant and give rise to metastases which are represented in the areas of "neuroglia cell rosettes," usually regarded as a stage in the development of the sclerotic plaque. Such a condition occurs in the so-called acute cases of multiple sclerosis.

The elements which enter into the formation of secondary lesions, that is, the lesions caused by impeded circulation and consequent parenchymatous degeneration with secondary reaction in the supporting tissue, are identical and characteristic of such a process in other conditions. Thus, various elements which enter into the pathology of multiple sclerosis (the undifferentiated cells, tracing the development of the primary lesion from such a cell, the elimination of the stage of "fat-granule cell myelitis" from this process, the successive stages of the secondary lesions which are identical with lesions following similar circulatory disturbances in other conditions, the occurrence of the two types of lesions and the distribution of these, the presence of mitotic cell division and binucleated ganglion cells) form an unbroken chain of evidence that the primary lesion of the disease originates in embryonal neurocytes of misplaced neuroblastic tissues. The fact that

the primary lesion of multiple sclerosis is a neuroglia fiber formation, and the new growth associated with it is a nerve fiber formation supports the assumption that the sheath of Schwann cells are the fiber-forming cells, either nerve fibers or neuroglia fibers, and the displacement of the mother cell to the central nervous system by the ingrowing vessel carrying connective tissue is in accord with the findings in the cases under discussion.

(The pathologic physiology of the disease will appear later in another paper.)

PLATE 6.—PERIVASCULAR PRIMARY PLAQUE FORMATION IN SPINAL CORD

Fig. I.—Cross-section showing primary lesion in a vessel of the postero-lateral septum of the spinal cord representing early stage of development. Lumen of vessel (5). Fiber forming neuroglia cell (8). Large neuroglia nucleus (15). Mitotic neuroglia (18). Van Gieson stain.

Fig. II.—Later stage from the same locality as Figure I, showing transformation of cells and neuroglia fiber formation. Lumen of vessel (5). Fibers forming neuroglia (8). Undifferentiated cell (17). Van Gieson stain.

Fig. III.—Later stage showing well developed neuroglia fiber proliferation. Fiber forming neuroglia (8). Pathologic neuroglia (10). Undifferentiated cell (17). Mitotic neuroglia (18). Van Gieson stain.

Fig. IV.—Showing well advanced fiber formation under higher magnification. Fiber forming neuroglia (8). Pathologic neuroglia (10). Undifferentiated neuroglia cell (17). Van Gieson stain.

PLATE 6

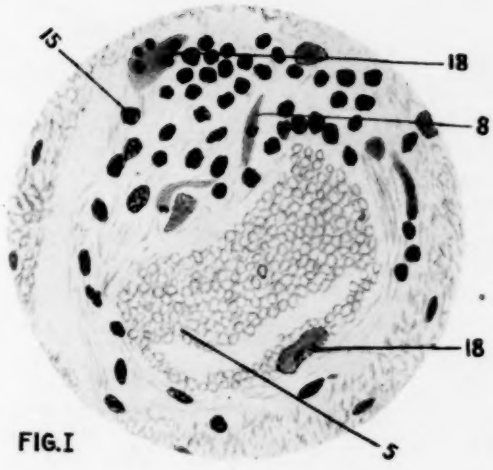


FIG. I

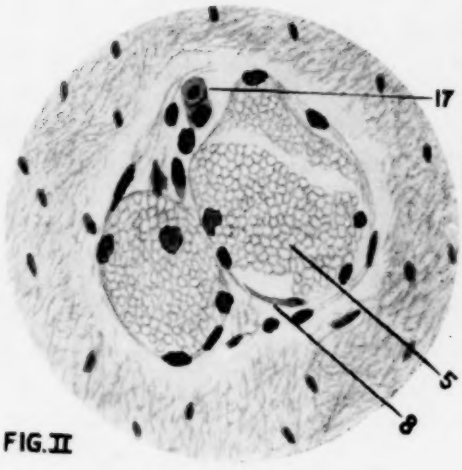


FIG. II

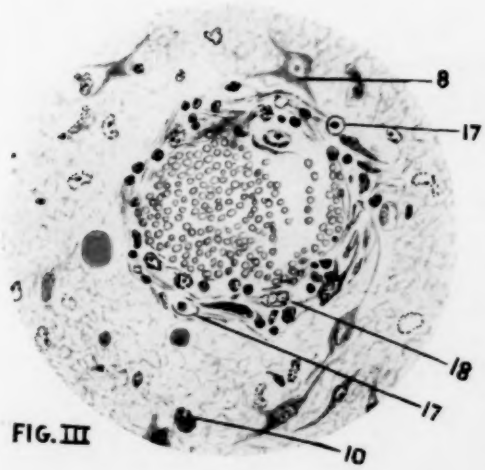


FIG. III

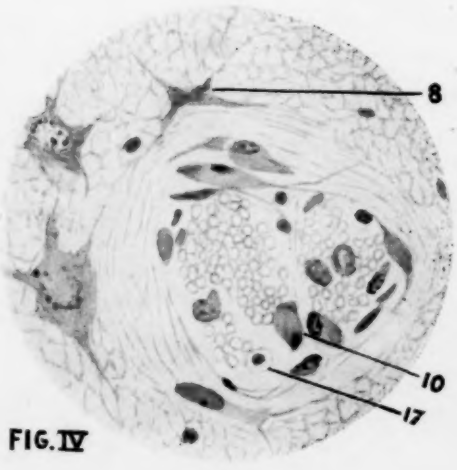


FIG. IV

PLATE 7.—PRIMARY PLAQUES SHOWING ARRANGEMENT OF NEUROGLIA FIBERS

Fig. I.—Primary plaque from cerebral cortex showing advanced glia fiber formation. Note radiating arrangement of fibers within the plaque and reticular arrangement of glia fibers in the surrounding tissue. Axis cylinder (39). Alzheimer method.

Fig. II.—Primary plaque from cerebral cortex more advanced stage. Note the homogeneous center and the arrangement of the marginal fibers in contrast with the surrounding reticular arrangement. Pathologic neuroglia cell (10). Blood vessel (38). Van Gieson stain.

Fig. III.—Numerous primary plaques from left lenticular nucleus under lower magnification. New capillary (38). Alzheimer method.

Fig. IV.—Primary sclerotic plaques from spinal cord. Demyelinated areas (42). Neuroma (43). Bielschowsky method.

PLATE 7

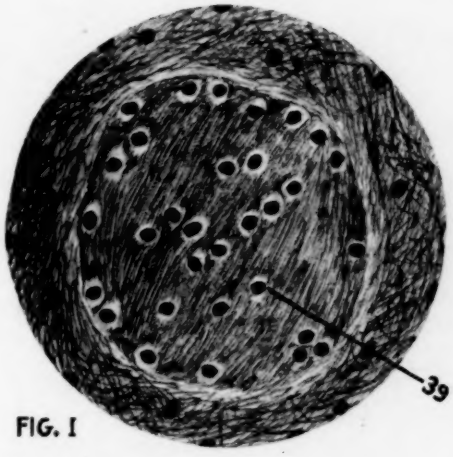


FIG. I

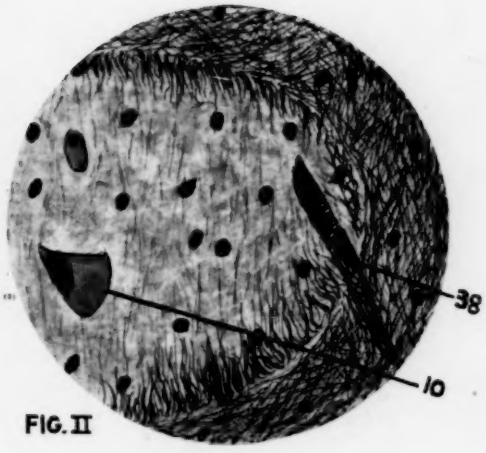


FIG. II

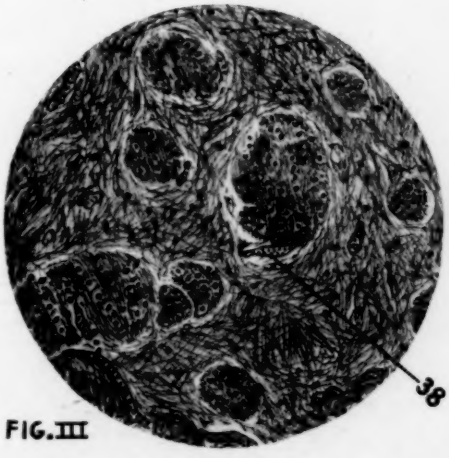


FIG. III

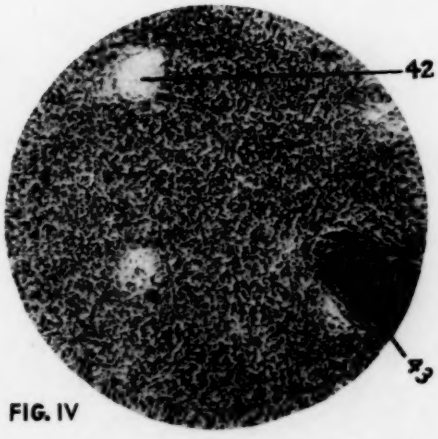


FIG. IV

Plate 8

Fig. I.—Blood vessel with mononuclear cell infiltration of vessel wall and perivascular tissue. Van Gieson stain.

Fig. II.—Section of a blood vessel showing demyelinization and perivascular glia proliferation with connective tissue increase. (Note persistent axis cylinders and perivascular areolar zones.) Van Gieson stain.

Fig. III.—A section through the aqueduct of Sylvius near the origin of the nucleus of the trigeminus showing granular ependymitis and a primary plaque. Primary plaque (40). Granular ependyma (41). Mallory's phosphotungstic acid hematoxylin.

Fig. IV.—Cross-section of cervical cord showing a sharply circumscribed sclerosed area (23) in the posterior column with more or less diffuse sclerosis about it. Pal-Weigert stain.

PLATE 8

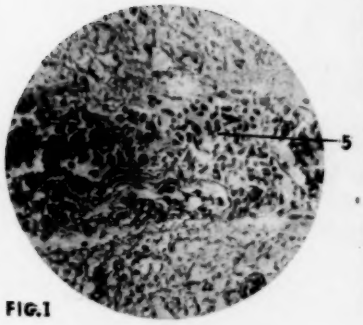


FIG. 1

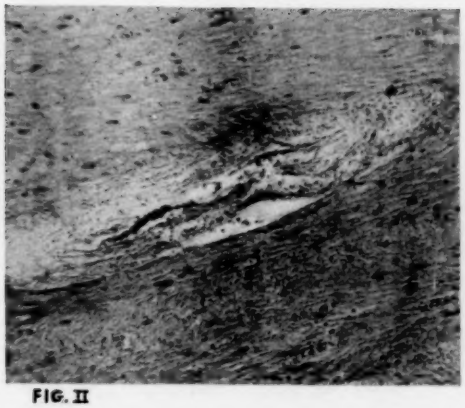


FIG. II

FIG. III

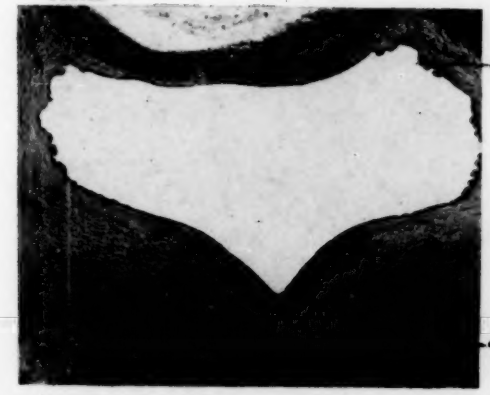


FIG. IV

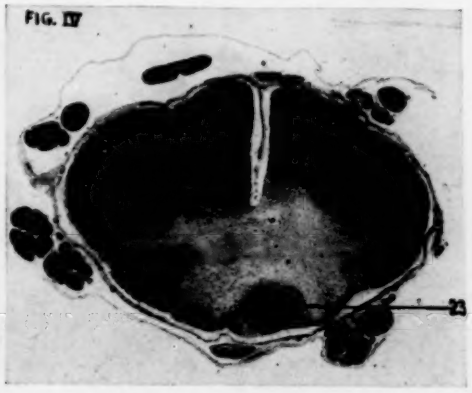


Plate 9

Fig. I.—Section of a cortical area showing numerous engorged capillaries and large areas of demyelination. Perivascular sclerosis (42). Bielschowsky's silver impregnation.

Fig. II.—Cross-section of a cortical area showing changes in the axis cylinders in the demyelinated area and the transition zone. Bielschowsky's silver impregnation.

Fig. III.—Section of cortex showing sievelike area. Mallory's phosphotungstic acid hematoxylin.

Fig. IV.—Section of cortical area showing advanced secondary sclerosis and small areas of softening. Bielschowsky's silver impregnation.

PLATE 9

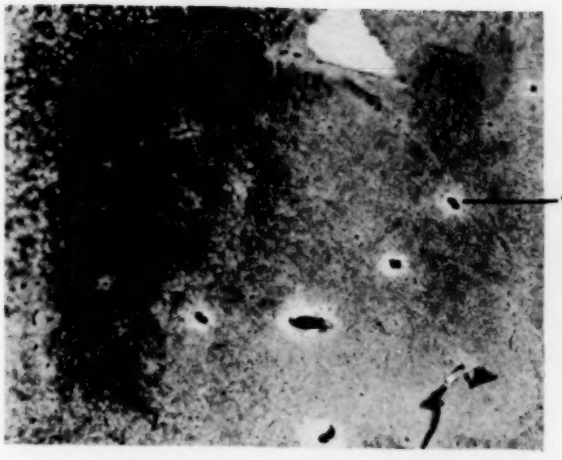


FIG. I

FIG. II

FIG. III

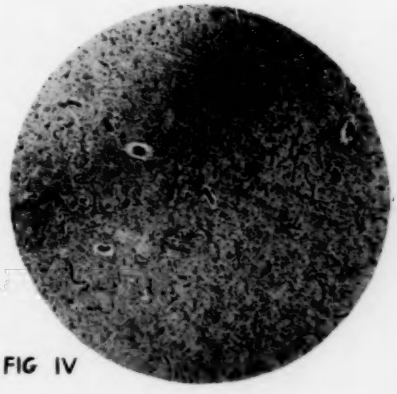


FIG IV

PLATE 10.—A STUDY OF THE VARIOUS CELL TYPES FOUND IN MULTIPLE SCLEROSIS

(17). Undifferentiated cell showing variations in the nucleus and cytoplasms.

(10). Pathologic neuroglia cell.

(43). Ameboid and granular neuroglia cells.

(34). Embryonic type of cells from the sheath of Schwann and from areas in the spinal cord.

(118). Mitotic neuroglia cell.

(8). Fiber forming neuroglia cell.

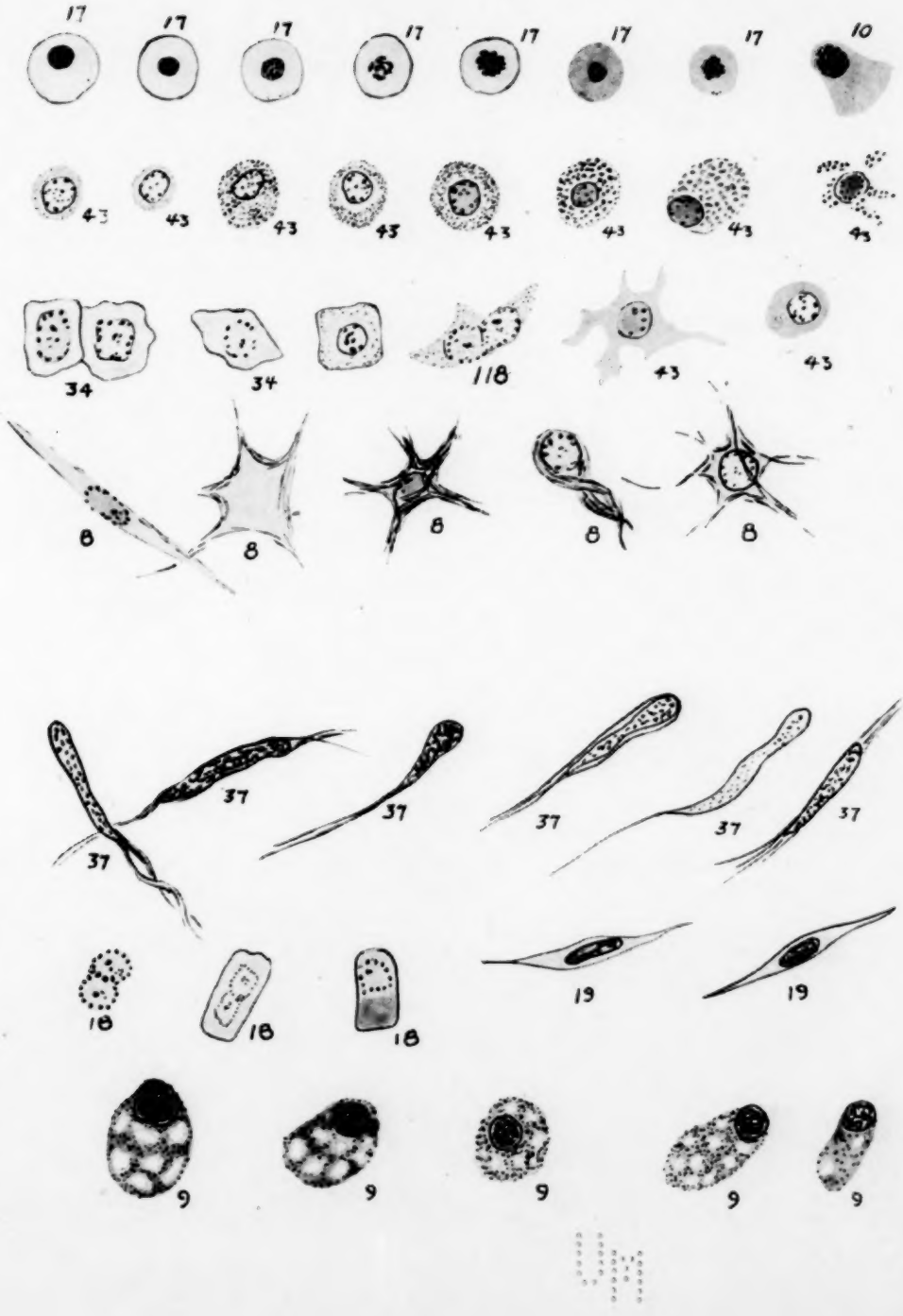
(37). Neuroblasts.

(18). Epithelioid cells.

(19). Fibroblasts.

(9). Fat granule cells.

PLATE 10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THE SUBACUTE FORM OF MULTIPLE SCLEROSIS*

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PHILADELPHIA

In order to obtain a more correct understanding of the histology of multiple sclerosis it is necessary to examine the lesions when the course of the disease has been rapid. Cases of multiple sclerosis with necropsy are exceedingly rare in America, and therefore one in which death occurred within the second year after the onset, as it did in the case presented in this paper, should be of interest. This study permits me to conclude that, at least in some cases, multiple sclerosis may be regarded as multiple glioma. There is also a possibility that at times syphilis may play a rôle, and opportunity is taken to consider the findings justifying this point of view.

The patient who afforded the opportunity for the present study was a male, aged 25. The symptoms began in February, 1915, with headache. In June, 1915, vision began to fail. In July, 1915, optic neuritis was observed. Weakness of the limbs developed gradually, with nystagmus, incoordination, vertigo, scanning speech, intention tremor and progressive impairment of gait until walking finally became impossible and mentality very feeble. Death occurred Dec. 21, 1916

The notes of this case are as follows:

History.—E. B., white man, aged 25, was admitted to the University Hospital of the University of Pennsylvania, July 21, 1916, and died Dec. 21, 1916. He had been well until February, 1915, when he began to have severe frontal headache. At this time he had no motor symptoms. In June, 1915, his vision began to fail. In the middle of July, 1915, he was admitted to the University Hospital on Dr. de Schweinitz's service. The diagnosis of optic neuritis was made. As vision failed the headache subsided. The sensation of twitching of the arms and legs grew worse and he became weak. He was greatly improved by one month's stay at the seashore. Since January, 1916, his condition has become steadily worse. In February, 1916, he developed ataxia of the lower limbs and vertigo, and the weakness of the lower limbs increased. His speech has become somewhat slurring, nasal, and monotonous since March, 1916. Since May he has had an intention tremor of the forearms. Since June 20, 1916, he has not been able to walk.

He has had chickenpox, whooping cough, influenza in infancy and early childhood. He denies venereal disease. His family history is negative. He does not use alcohol. He is a student in the Wharton School of the University of Pennsylvania.

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* Read by title at the Annual Meeting of the American Neurological Association, May, 1917.

Examination.—The pupils are equal; irides react promptly and equally to light and in convergence. Horizontal nystagmus of large amplitude occurs when he looks to either side, and vertical nystagmus when he looks upward. Extraocular rotations are unimpaired. Facial musculature is unimpaired. Hearing of the watch tick is fair in each ear. The tongue is protruded slightly to the right of the midline without tremor and is freely movable to either side.

Extremities: Grip fair with the right hand, poor with the left. Marked ataxia and, at times, course intention tremor developed in both arms by finger to nose and finger to finger tests. Diadochokinesis is impaired in both forearms. Sense of position and stereognostic sense are normal in the hands. Biceps reflex is normal and equal on both sides. Triceps reflex is questionably present on both sides. Cremasteric reflex is prompt on the left side, sluggish on the right. Patellar reflex is slightly exaggerated on the right side, normal on the left. Achilles reflex is moderate on both sides and equal. Plantar stimulation induces plantar flexion on the left side, dorsal flexion on the right side. Ankle clonus was obtained on the right side at the first examination, but could not be elicited on either side at the second examination. Heel to knee test shows marked ataxia on both sides. Both legs show slight spasticity. Legs and trunk are weak and probably ataxic. The man cannot stand or even sit up unsupported. Sensations of touch and pain are normal throughout. Slight coolness is mistaken for warmth in the right calf. Otherwise objective sensation is unimpaired.

The voice is slow, monotonous, thick and somewhat slurring. The laugh is deep, expressionless, almost spastic, not unlike the laugh of Wilson's disease. The lower limbs are very weak. There is more power in extension than in flexion. There are frequent brief rapid changes in the amount of power in all the movements of the extremities. He passpoints outward with both hands spontaneously.

July 25, 1916: (Ocular report by Dr. Langdon.) O. D., vision 6/15; O. S., 6/45. Both disks show decided loss of capillarity, well defined central cups and sharply defined margins. There are no other fundus changes.

July 22, 1916: Blood: Red blood cells, 5,160,000; white blood cells, 8,400; hemoglobin, 80; polymorphonuclears, 78; lymphocytes, 19; large mononuclears, 1; transitionals, 1; eosinophils, 1; basophils, 1. Urine analysis: Cloudy, amber-colored; flocculent sediment; specific gravity, 1.025; acid reaction; albumen, none; sugar, none; casts, no cylindroids; mucus, plus; no red blood cells; white blood cells, occasionally present; epithelium was present, also calcium oxid crystals.

July 28, 1916: Lungs are negative except for slightly increased vocal fremitus over the right upper lobe. Heart is negative except for slightly accentuated pulmonic second sound.

Sept. 18, 1916 (ocular report dictated by Dr. Shumway): There is a marked pallor of the temporal half of the optic nerve on each side and paralysis of the right internal rectus.

Oct. 10, 1916: Patient is somewhat delirious. Wassermann test of the blood has been taken several times in the hospital and was always negative. The patient's father states that the blood taken outside the hospital for the Wassermann test he thinks was positive. Owing to certain circumstances a lumbar puncture was not done.

Oct. 13, 1916: The patient is not able to take care of himself and lies in bed except when moved in a wheeling chair. He has marked ataxia, scanning

speech, nystagmus and intention tremor. His mentality has gradually failed and is now greatly impaired.

Dec. 21, 1916: This morning the patient's temperature, pulse and respiration suddenly went up above normal and he could not be aroused. He had been without change in his condition on retiring the night before. His heart was fast and irregular. At 8 a. m. on this date he was still unconscious and his breathing was difficult and irregular, and, while still fast, there was no increased area of cardiac dulness.

Postmortem Examination (Dec. 21, 1916).—The postmortem examination revealed practically nothing abnormal with the viscera. The areas of sclerosis are very numerous and are found in every section taken from the spinal cord, but they are more pronounced in the cervical and lumbar regions than in the thoracic. These areas are in some places fairly sharply defined from the normal tissue, but in many places the shading off into normal tissue is observed. Lacelike structure is found in some of the patches. The areas are infiltrated with numerous mononuclear cells, and these are especially numerous about the blood vessels within the cord and in some of the septa running into the cord. These cells are very numerous in both the pia of the cord and brain, and in some places form dense masses. The large spider cells (Deiters' cells) so numerous in the foci within the cerebrum, are not found in the cord.

The alteration in the medulla oblongata is as intense as in the cord. The Marchi sections of the cord and brain show intense recent degeneration except in areas of long standing in the cord. The nerve cells of the anterior horns of the cervical and lumbar regions are well preserved even in sclerotic foci, as shown in the thionin stain, and do not show pigmentary degeneration, although occasionally a cell showing chromatolysis and swelling may be found.

The optic chiasm, tracts and nerves are greatly degenerated and show much infiltration with cells of mononuclear type. Some foci of degeneration are found in the cerebellum, as in the right dentate nucleus.

Sections from many parts of the cerebrum show disappearance of medullary substance in the altered areas. The sharpness of definition of the degenerated from the normal tissue is possibly even more pronounced here than in the spinal cord. The nerve cells in the altered cortex are well preserved. The cerebral foci contain many large glia cells (Deiters' cells), mononuclear cells and fatty granular cells, and these foci differ greatly from the foci of the spinal cord in that the former are almost entirely cellular. These areas look like so many distinct gliomas, and while they appear under low power to be sharply defined, under high power scattered glia cells may be seen penetrating into the adjacent tissue like scouts of an invading army.

There have been few cases of multiple sclerosis with necropsy reported in this country — a statement also made by Taylor — and the study of this disease must be made chiefly from the foreign literature. There we find cases in which the brain has been seriously affected by the lesions, but in most cases the description has been based on the study of the spinal cord. In this case of subacute multiple sclerosis recently under my care every section taken from any part of the cerebrum shows foci with lesions peculiar to this disease. The alteration in the cerebrum is very different from that in the spinal cord, and my findings confirm the statement of Marburg, namely, that cellular

proliferation of glia is greater in the brain than in the spinal cord, and that the large glia cells are found more in the brain than in the spinal cord.

The glia proliferation of the spinal cord is in large measure of the character of the overgrowth of glia seen in the replacement of nerve fibers from secondary degeneration caused by some lesion at a higher level; it is therefore chiefly fibrillar. In the cerebrum the glia proliferation is of a different character, it is chiefly cellular and is more recent than that of the cord. Mental failure usually does not precede the other symptoms of multiple sclerosis, it occurs later in the disease

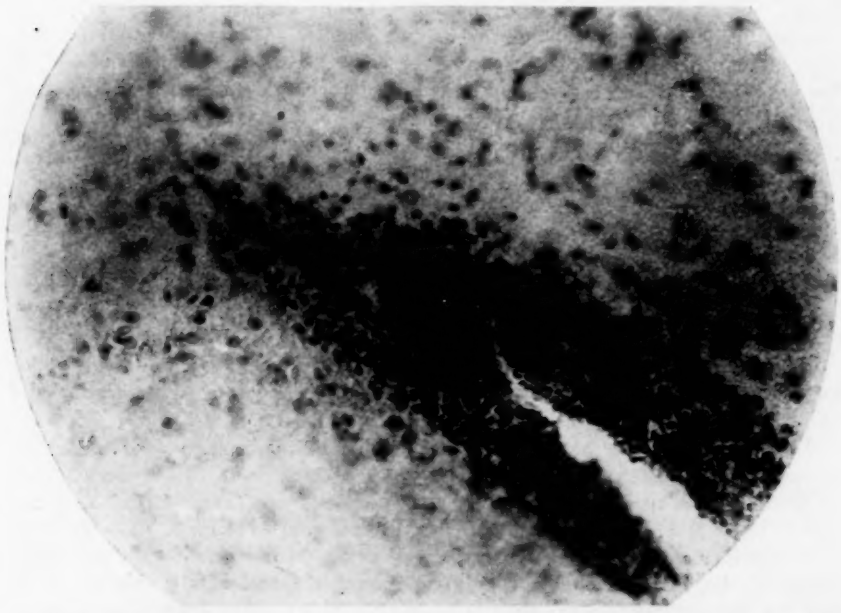

Fig. 1.—Vessel in the left paracentral lobule surrounded by many cells of mononuclear type.*

and the lesions producing it must be of late development. In this case the mental failure became pronounced and it is to be explained by the extensive alteration of the cerebrum. If one, therefore, desires to find the earlier changes of multiple sclerosis he should look for them in the cerebrum. The lesions are usually less numerous in the cerebellum.

The changes in the cerebrum in the case recorded in this paper were in overgrowth of the glia causing a microscopic picture resembling that of a glioma. Indeed, my studies of these sections lead me

*I am indebted to Dr. A. J. Smith for the photomicrographs.

to conclude that multiple sclerosis may be a process consisting of innumerable minute gliomas, although other types possibly may occur. It is no wonder, therefore, that the mentality of my patient became exceedingly feeble. The cellular infiltration of mononuclear type within the tissue about the vessels has been noted in many cases of multiple sclerosis, but it may be found also in glioma. The large glia cells, spider cells or Deiters' cells, I have found only in the brain, and they are indicative of chronic irritation. I have seen them in the spinal cord when the cord was severely distorted by the pressure

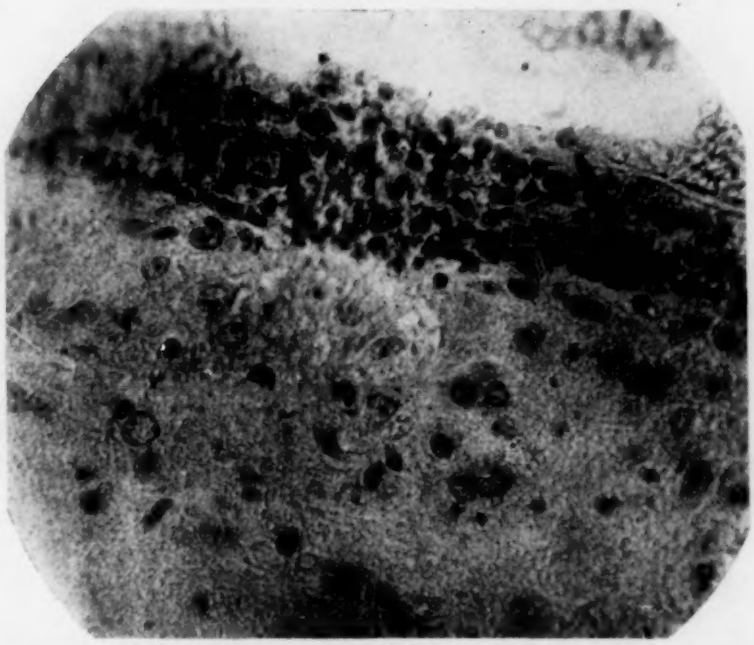

Fig. 2.—Part of the vessel shown in Figure 1 under higher magnification. Beyond the mononuclear cells are seen numerous other cells, some of which are glia cells.

of an extramedullary tumor, but I have not observed them to the same degree in syphilitic encephalitis.

The relation of the foci to blood vessels has been asserted by some investigators, disputed by others—I have not been able to establish it. About one vessel within the brain many mononuclear cells were found and beyond these were other cells, some of which evidently were glia cells. It seems as though some irritative substance either within the vessel or the perivascular sheath may have caused this proliferation (Fig. 2).

Wohlwill made a very thorough digest of the literature of multiple sclerosis for the ten years ending April, 1913. He says the definition of multiple sclerosis is made to include different lesions by different writers. From a pathologic viewpoint he defines the condition as the occurrence of circumscribed foci in the central nervous system in which the medullary sheaths have disappeared or are disappearing, the axis cylinders and ganglion cells are relatively intact, and a more or less intense glia proliferation exists without displacement of the adjoining nervous tissue. Siemerling and Raecke have stated that in those cases in which the cerebral cortex is implicated the cortex is the

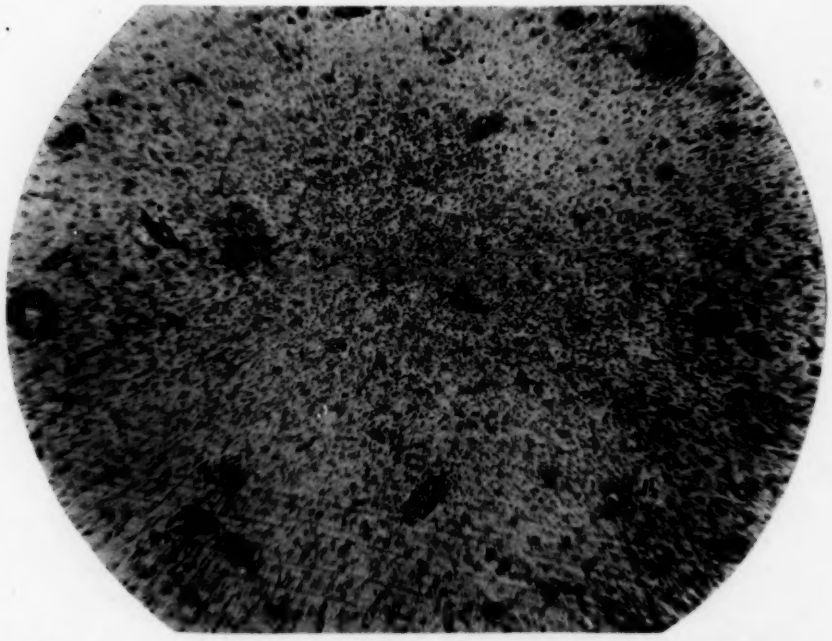

Fig. 3.—A mass of proliferated glia cells included entirely within a low magnification, showing the small size of some of the altered cerebral areas.

chief seat of the lesions, but my examination in this case does not support this statement. Cases with great preponderance of cortical involvement he states have been reported by Dinkler, Fuller, Klopp and Jordan.

The most recent comprehensive work on multiple sclerosis has been done by James W. Dawson. He states that the etiology of the disease remains absolutely obscure. The supposition of a selective poison acting through the blood vessels, which has received the support of most recent investigators, is justified as an hypothesis, but remains undemonstrated as a fact. Dawson devotes special attention to the

early changes of the disease, and he states that our knowledge of the histology, especially of the early stages, has not kept pace with our recognition of the early clinical aspects of the disease. Experimental investigation, Dawson says, has proved only that disseminated areas of myelitis may result in a reparative growth of neuroglia, but it has not proved that area of typical disseminated sclerosis proceed from an acute myelitis.

I am unable to accept the view that multiple sclerosis is caused alone by some irritant circulated by the blood, but it seems to me

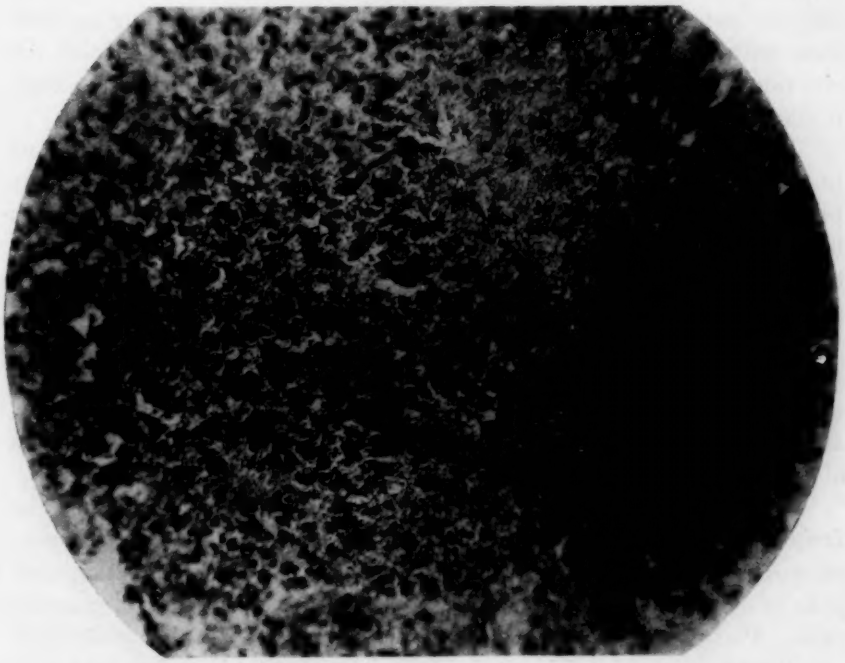

Fig. 4.—One of the cerebral sclerotic areas consisting largely of glia cells, under higher magnification than that represented in Fig. 3. The sharp definition of normal from altered tissue runs almost through the middle of the photograph. Mallory's neuroglia stain.

probable that such an irritant acting on tissue in which the disease is latent may hasten its development.

Dawson asserts that a study of the cerebrospinal fluid in multiple sclerosis has as yet thrown little light on the disease, but investigations along this line have not been extensive.

In the report of a case of multiple sclerosis he states that the "early" areas in the cerebrum consisted largely of closely arranged fatty granular cells between which were large protoplasmic, proliferated glia elements; of dilated vessels, with fatty granular cells and

other nucleated elements in their adventitial spaces; of markedly altered persisting axis cylinders; and of a gradual transition zone in which these changes were less marked and in which degenerating myelin fibers were found. These findings describe very accurately those in my case.

Dawson found the cerebral and spinal meninges almost normal in his uncomplicated cases; meningeal changes when present were diffuse and in no way confined to the meninges overlying areas of sclerosis.

As for syphilis, he says it has no significance in the etiology. Syphilis may produce disseminated areas in the central nervous system, but the histologic character of these have, as a rule, nothing in common with those of disseminated sclerosis, in which disease also the reactions of the serum and cerebrospinal fluid and the cytologic examination of the spinal fluid are all negative.

The cellular infiltration of mononuclear type in the cerebral pia in my case is a finding of considerable interest. It is exceedingly pronounced and suggests the findings of syphilis. Unfortunately, a lumbar puncture in this case was prevented by certain circumstances, but a Wassermann test of the blood done outside the hospital was supposed to be positive.

When working in Obersteiner's laboratory in 1893 and 1894, I found in a case of multiple sclerosis cell infiltration of mononuclear variety of considerable intensity about the blood vessels of the cord and within the spinal pia. This finding is referred to by Bikeles in his paper published in 1895.

Wohlwill, in his critical digest on multiple sclerosis, speaks of the frequency of the perivascular cellular infiltration, but says polymorphonuclear cells do not occur in the infiltration. The infiltration consists of lymphocytes, plasma cells, some mast cells and fatty granular cells. Plasma cells are not always present. The cellular infiltration usually does not extend beyond the perivascular limiting layer of glia, although lymphocytes occasionally are found within the degenerated focus.

The meninges he states frequently are thickened and may show cellular infiltration, consisting of lymphocytes, plasma and mast cells, endothelial and connective tissue cells, and the vessels may show similar changes to those of the vessels within the foci. The cellular infiltration about the vessels of the pia he states is described by Flatau and Kölichen.

Marburg in his paper on acute multiple sclerosis stated that the meninges in acute multiple sclerosis had not received so much attention as they deserve. In one case only he found meningeal changes. Cellular infiltration was chiefly with connective tissue cells, but also with endothelial cells from the vessels, mast cells, plasma cells and

lymphocytes, but the picture he gives does not show anything like the intensity of cellular infiltration seen in my case.

Rönne and Wimmer found in a case of acute multiple sclerosis pronounced cellular infiltration of the tissue, either diffuse or in little clumps, especially about a vessel or within its walls. The cells were mononuclear and polynuclear leukocytes, fatty granular cells, plasma cells and *Stäbchenzellen*. They found no evidence of spinal meningitis. They give much evidence justifying the opinion of multiple sclerosis as a myelitis—an inflammatory process.

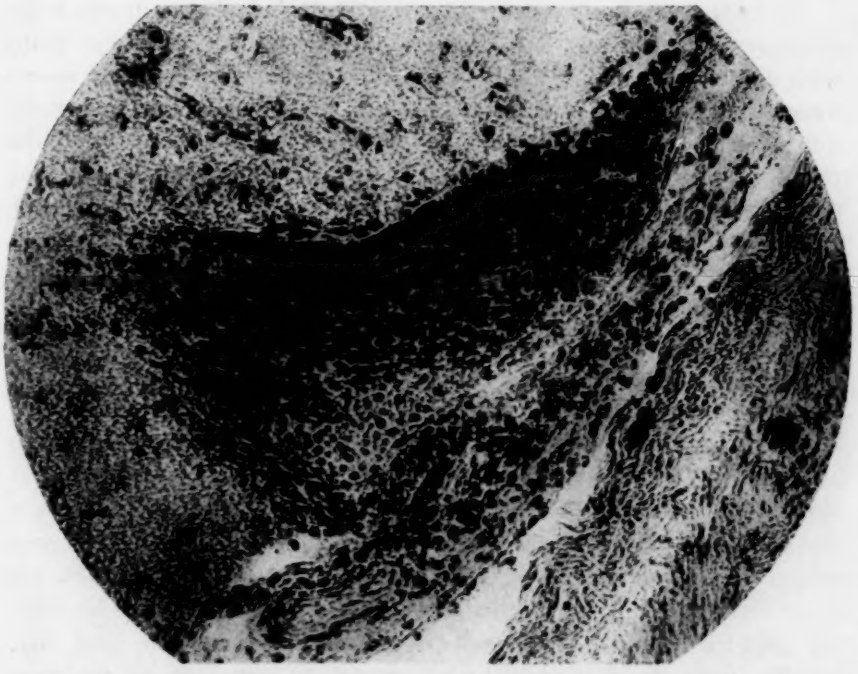

Fig. 5.—Large collection of mononuclear cells in the pia of the left paracentral lobule, suggesting the finding of syphilis.

In a case of multiple sclerosis described by Finkelnburg the vessels in the foci were much distended and surrounded by broad masses of mononuclear cells, and in some places these cells hid the vessel walls, and in some places the tissue surrounding the vessels was infiltrated with the round cells, but there was no sign of meningitis. He found an infiltrated vessel in the midst of a focus, as a rule, and he states that in his case, as in Ribbert's and Goldscheider's, an infiltrated vessel was found in the center of most of the small foci. Finkelnburg found many vessels infiltrated with round cells that were not in sclerotic foci.

The case reported by Barbier and Gassier was in a child 5 years of

age, in whom the Wassermann reaction was positive, and the symptoms these authors thought could be attributed only to multiple sclerosis. Much improvement occurred in the child's condition. The case was without necropsy and is not altogether convincing, and does not prove that the condition was caused by syphilis.

Dr. Joseph McIver at my request has examined the fluid obtained by lumbar puncture from a typical case of multiple sclerosis of a few years' duration. He found 200 cells to the cubic millimeter, mostly mononuclear. An accident prevented a Wassermann examination of this fluid.

In 1909, I reported with Dr. Andrew H. Woods a case in which the symptom complex was one of spastic paraplegia of the lower limbs with contracture of the limbs, and pain produced by passive movement of these limbs, probably because of the contractures; exaggeration of tendon reflexes in both upper and lower limbs, although the reflexes could not be well demonstrated in the latter because of the position of these limbs; and loss of control of bladder and rectum, with preservation of objective sensation. These symptoms could be caused by multiple sclerosis.

Numerous areas of sclerosis were found throughout the cervical and upper thoracic regions of the cord, some of which resembled closely the degenerated areas found in multiple sclerosis. Slight cellular infiltration of mononuclear type in the pia, the gradually shading off of the sclerotic areas into the normal tissue instead of the sharp line of differentiation; the vascular and perivascular sclerosis in regions of the cord where there was no distinct focus of sclerosis, seemed to us to indicate that the process was syphilitic. I feel less sure of the correctness of this viewpoint at the present time, and am almost willing to accept Catola's opinion that the distinction between the different forms of multiple sclerosis are unreliable and that syphilis cannot be eliminated as a cause. It is well to recall the view of Orlowsky, and Thomas and Long, that syphilis and multiple sclerosis have occurred in the same person.

Wohlwill states that the pathologic distinction between multiple sclerosis and the multiple lesions of syphilis in many cases is not simple. The syphilitic lesions may be very similar. Barbier and Gassier try to establish a relation between certain cases of multiple sclerosis of childhood and congenital syphilis. Marburg has stated that he has found multiple sclerosis strikingly frequent in the descendants of syphilitic parents, even when the patients presented no evidence of syphilis. Statistics have not shown that syphilis is frequent in the history of multiple sclerosis cases. Berger found it only in 1.5 per cent. of the cases, Klausner in about 3 per cent. Hauptmann in

a comparatively short time found four cases of multiple sclerosis with syphilitic history.

Catola states that in certain cases syphilis is the only malady which seems to play a rôle in the etiology of multiple sclerosis, and refers to Babinski, Greiff, Orlowsky, Thomas and Long, and Wernicke, but concludes that the relation of syphilis to multiple sclerosis is far from being determined.

In the first case of Catola's paper the patient is said to have been syphilitic and had disseminated lesions which Catola regarded as like those of multiple sclerosis. The spinal pia was infiltrated by lympho-

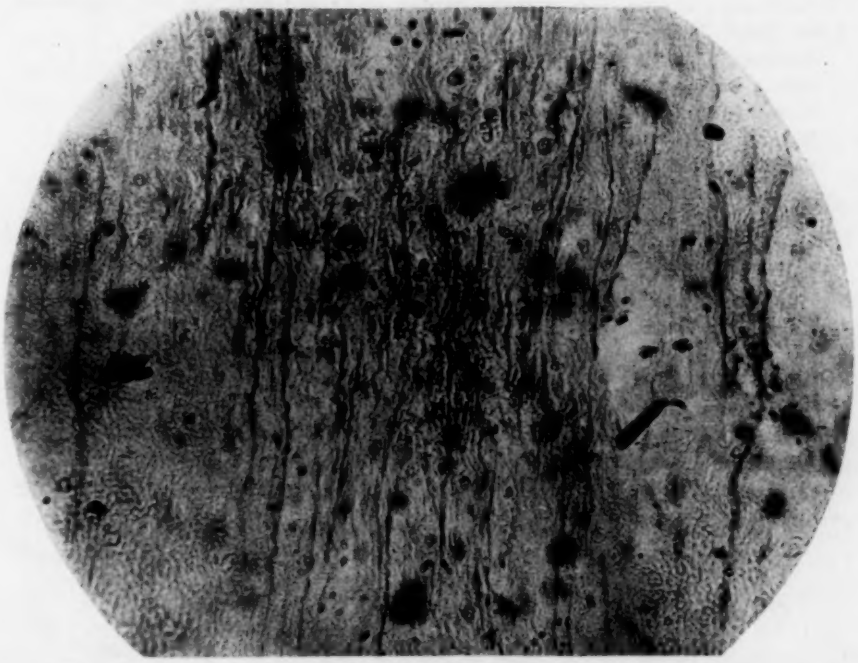

Fig. 6.—Naked axis cylinders (Bielschowsky stain) in a sclerotic area of the spinal cord, showing the presence of these axis cylinders in apparently completely degenerated tissue.

cytes and polynuclear cells, and the infiltration was especially intense in the posterior longitudinal septum. The photographs represent an intense cellular infiltration of the pia. The polynuclear cells were found almost exclusively in the lower part of the cord and were attributed to infection from a bedsore. Catola concludes that syphilis may be very important in multiple sclerosis, and there is a syphilitic multiple sclerosis like a multiple sclerosis of any other infectious origin.

It seems probable that syphilis has some influence over multiple sclerosis. The typical lesions probably are not syphilitic in character, but the syphilis may be an *agent provocateur*. It would be well to treat early cases of multiple sclerosis as possibly syphilitic—the therapeutic test is well worthy of trial.

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Kuhn and Steiner (Med. Klin., No. 37, 1917), by inoculating rabbits and guinea-pigs with blood and cerebrospinal fluid from cases of multiple sclerosis produced paralysis and found spirochetes within the vessels of the liver of the inoculated animals.

Siemerling (Berl. klin. Wchnschr., No. 12, 1918) discovered living spirochetes in the sclerotic foci of multiple sclerosis.

Strümpell (Neurol. Centralbl., No. 12, 1918) urges caution in the interpretation of these findings.

UNSUSPECTED INVOLVEMENT OF THE CENTRAL NERVOUS SYSTEM IN SYPHILIS

A STUDY OF SIX HUNDRED AND TWENTY-FOUR UNSELECTED CASES *

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Within recent years it has been gradually established that syphilis in the early stages may cause marked lesions of the central nervous system, but it has been more slowly realized that it may also produce definite involvement of the central nervous system without necessarily causing any symptoms.

Since 1903, when a series of papers by Ravaut[1] appeared, much interest has been shown in the study of this phase of the disease. Ravaut examined the cerebrospinal fluid of 100 cases of early secondary syphilis, and found pleocytosis and other pathologic changes in many. In fact, only twenty-eight could be said to be normal. Other similar observations made on small series of cases were reported by Boas and Lind,[2] Zaloziecki and Frühwald,[3] and Bergl and Klausner.[4]

In 1913, Altmann and Dreyfus[5] published the results of the exam-

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* This subject is discussed in greater detail in a paper by the same authors entitled "The Occurrence of Unsuspected Involvement of the Central Nervous System in Unselected Cases of Syphilis," Brain, Lond. **41**:255, 1918.

1. Ravaut, P.: Le Liquide Céphalorachidien des Syphilitiques en Période Secondaire, Bull. et mém. de la Soc. méd. d. Hôp. de Par. **20**:1026, 1903.

2. Boas, H., and Lind, H.: Untersuchungen der Spinalflüssigkeit bei Syphilis ohne Nervensymptome, Ztschr. f. d. ges. Neurol. u. Psychiat., O. **4**:6, 1911.

3. Zaloziecki, A., and Frühwald, R.: Zur Kenntnis der Hirnnervenstörungen im Frühstadium der Syphilis, Speziall nach Salvarsan, Wien klin. Wchnschr. **25**:1162, 1912.

4. Bergl, K., and Klausner, E.: Ueber das Verhalten des Liquor Cerebrospinalis bei Luetikern, Prag. med. Wchnschr. **37**:467, 1912.

5. Altmann, K., and Dreyfus, G.: Salvarsan und Liquor Cerebrospinalis bei Frühsyphilis, nebst Ergänzenden Liquoruntersuchungen in der Latenzzeit, München. med. Wchnschr. **60**:464 and 531, 1913.

ination of the cerebrospinal fluid in 170 cases, which included all stages of syphilis. They found in the "secondary stage with chancre," 5 abnormal out of 21; in the "secondary stage without chancre," 21 abnormal out of 35; and in the "latent stage," 10 out of 19 were abnormal. These fluids all had over 15 cells per cubic millimeter, and some gave a positive Wassermann reaction. They also showed that the abnormalities could be reduced by arsphenamin treatment.

In the same year Ellis and Swift[6] and Gamper and Skutezky[7] reported similar findings, while Engman, Buhman, Gorham and Davis[8] appear to have been the first to make a routine examination of unselected cases. Wile and Stokes[9] also made routine examinations of all syphilitics and laid special emphasis on their observations that impaired bone conduction and "neuroretinitis" were usually present when the cerebrospinal fluid was abnormal. Of six cases of primary syphilis they found "neuroretinitis" in five, but did not discuss their findings in detail. In 1914, Hauptmann,[10] Leopold,[11] Gutmann,[12] and Audry and Lavau[13] may be added to the list of those who placed on record that cerebrospinal fluid abnormalities do occur in cases of early syphilis.

RECENT INVESTIGATIONS

The most recent and extensive paper on the subject was written by With[14] in 1916 and published two years later. In his series of 316 cases of syphilis of all stages, twenty-six, or 12 per cent., had a

6. Ellis, A. W. M., and Swift, H. F.: The Cerebrospinal Fluid in Syphilis, J. Exper. Med. **18**:162, 1913.

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11. Leopold, O.: Ueber Nervensymptome bei Frischer Syphilis, Arch. f. Dermat. u. Syph. **120**:101, 1914.

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13. Audry, Ch., and Lavau: Sur les Méningites Preroséliques, Ann. de dermat et de Syph. **5**:29, 1914-1915.

14. With, C.: Studies on the Different Reactions (Lymphocytosis, Bisgaard, Ross-Jones and Wassermann) in the Cerebro-Spinal Fluid in Cases of Syphilis, Brain, Lond. **40**:403, 1918.

pathologic increase of cells (10 or over) in the cerebrospinal fluid. Of these, 134 with rashes when examined from three to five months after infection showed 10 per cent. with abnormal cell count. It is not quite certain to what extent this series is unselected; and as there is no clinical description of the cases it is difficult to satisfy oneself regarding the one instance quoted of a case of primary syphilis which had a slight positive Wassermann reaction in the cerebrospinal fluid. The fluid contained no cells and the serum Wassermann was negative. It is thus evident that among syphilitics, particularly those in the early stages of the disease, there is a considerable percentage who have definitely pathologic changes in the central nervous system, and others with fluids less abnormal, who may be said to have doubtful changes. Indeed, this is as one would expect, for as Lang stated in 1881, "an organ which is the seat of a gummatous lesion must have been affected in the early period of syphilis."

McIntosh and Fildes[15] also pointed out in 1914, that the late central nervous system disease of syphilis might well be due to an invasion of spirochetes in the early stages, and argued that a tertiary syphilitic lesion was due to a recrudescence in a remnant of spirochetes which had remained dormant *in situ* since the generalization during the acute stage.

Obviously this matter has a most important bearing on the treatment of syphilis. If all cases of locomotor ataxia dementia paralytica are preceded by early involvement of the central nervous system which causes no symptoms, it is most important that they should be discovered as early as possible. It was with a view to determine the incidence of such involvement in the various stages of the disease, to observe the effect of treatment, and to discover if such cases require special treatment that this work was undertaken.

NATURE AND CLASSIFICATION OF CASES

We wish it to be distinctly understood that this series consists entirely of unselected cases, and is composed of men who were admitted in the ordinary way to the venereal section of this hospital. It does not include any instances of frank nervous disease which would have been admitted to the neurological section. We have made it so, that our results might be taken as typical of any similar collection of cases elsewhere.

For the purposes of the investigation we have divided our cases into six divisions and have abandoned the conception of primary,

15. McIntosh, J., and Fildes, P.: A Comparison of the Lesions of Syphilis and Parasyphilis, Together with Evidence in Favor of the Identity of These Two Conditions, Brain, Lond. **37**:141, 1914.

secondary and tertiary stages because syphilis is a progressive disease, the organisms become generalized soon after inoculation, and the various "stages" are inconstant and merge one into the other. The classification adopted is as follows:

CLASSIFICATIONS ADOPTED FOR PURPOSES OF STUDY

DIVISION 1: Cases diagnosed by finding *S. pallida* in an inoculation lesion, before the Wassermann reaction had become positive.

DIVISION 2: Cases with a positive Wassermann reaction which had as yet shown no signs of generalized infection other than glandular enlargement, up to and including twenty-six weeks from infection.

DIVISION 3. Cases with evidences or definite history of general infection (rash, etc.) up to and including eleven weeks from infection.

DIVISION 4: Cases similar to Division 3 but from twelve to twenty-six weeks, inclusive, from infection.

DIVISION 5: Cases with active lesions of syphilis over twenty-six weeks from infection.

DIVISION 6: Cases which had no active signs of syphilis over twenty-six weeks from infection.

In every case except two in our series, excluding Division 1, the Wassermann reaction in the serum was positive.

TECHNIC AND METHODS OF EXAMINATION

For the Wassermann reaction the cholesterinized alcoholic heart extract antigen of Fildes and McIntosh[16] was used throughout. The amount of serum used was 0.1 c.c. with amounts of reagents corresponding to 0.5 c.c. of a 5 per cent. suspension of sedimented sheep's blood cells.

The test as applied to the cerebrospinal fluid was done quantitatively in four tubes, the amounts of fluid used being 0.8, 0.2, 0.05, and 0.012 c.c. The fluid was *inactivated* at 56 C. for thirty minutes, the same as the serum. The reason for inactivating the cerebrospinal fluid was that such large quantities of it were used. It has been shown[16, 17] that there is a difference between the Wassermann reaction in the cerebrospinal fluid from dementia paralytica, and that in the fluid from a case of acute syphilitic meningitis. The reacting substances in the former are more thermostabile than in the latter, and it has been suggested that this is because the Wassermann producing substances are derived from two sources—in dementia paralytica from the central nervous system itself, and in the meningeal affection from the exudate from the blood stream as well. It is this material introduced direct from the blood stream as the result of meningeal inflammation which produces the difference, since normal serum unheated is itself capable in low dilutions of producing an inhibition of hemolysis. And, since in this work eight times as much cerebrospinal fluid is used as srum, a small amount of exudate in the cerebrospinal fluid, if unheated, would tend toward giving a falsely positive result. Since the true Wassermann producing substance is thermostabile, inactivation of the fluid while increasing the specificity of the test does not decrease its delicacy.

16. Fildes and McIntosh: The Wassermann Reaction and Its Application to Neurology, Brain, Lond. **36**:193, 1913.

17. McIntosh, J., Fildes, P., Head, H., and Fearnsides, E. G.: Parasyphilis of the Nervous System, Brain, Lond. **36**:1, 1913.

To express the results we have used figures throughout. In the serum, "4" means a positive reaction, "0" is used to denote a negative. Similarly, with the cerebrospinal fluid a figure is used for each of the four tubes. Where only one figure appears it always refers to the tube containing 0.8 c.c. of fluid. The figures "3, 2 and 1" are used to express partially positive results, and the sign "—" means that the test was not carried out.

The cell counts were usually done immediately after lumbar puncture but always within an hour. Tests for globulin were not made because we considered that for our purpose they would not furnish more information than could be obtained from the estimation of cells and the Wassermann reaction.

The nervous system of most patients with abnormal cerebrospinal fluids was examined as a routine. Symptoms were carefully inquired for; sensation was tested by a wisp of absorbent cotton and with the point of a pin; the functions of cranial nerves except taste and smell were examined, and the state of the reflexes, coordination, and the mental state when indicated, were noted. The eye-grounds were examined by the ophthalmic surgeon of the hospital—Surg. Lieut. Commander R. J. E. Hanson, R.N.V.R. The bone conduction was examined with the collaboration of Temp. Surg. Lieut. E. C. Dunlop, R.N., in charge of the otological department.

RESULTS OF THE EXAMINATION OF THE CEREBROSPINAL FLUID

In considering the cell content of the cerebrospinal fluid the question at once arises as to what number of cells is to be considered abnormal. Without going into details regarding the variations which may normally occur, and considering that it is better to err by having too few cases abnormal than too many, we believe we are following the consensus of opinion in considering 10 cells and over per cubic millimeter, pathological; from 5 to 9 cells (inclusive) per cubic millimeter, "doubtful"; and from 0 to 4 cells, normal. We have thus divided our cases into two groups — "positive" and "doubtful"— the former definitely pathological, the latter much more likely to be so than to be normal. The accompanying tables show the incidence of abnormal cases in each division.

TABLE 1.—INCIDENCE OF ABNORMAL CASES IN EACH DIVISION

Division	Number of Cases	With Positive Cells		With "Doubtful" Cells	
		Number of Cases	Percentage of Cases	Number of Cases	Percentage of Cases
1	71	2	2	9	12
2	168	15	8	17	10
3	107	18	16	11	10
4	85	25	29	11	12
5	78	14	17	11	14
6	115	41	35	14	12

Of the total number of cases we have found 18 per cent. are positive and 12 per cent. "doubtful"; and, if as we think likely, the latter are abnormal, 30 per cent. of all cases are pathological.

It also appears that a small percentage have a pleocytosis even before the Wassermann reaction in the serum becomes positive (Division 1). As the disease progresses this number increases until in the "late secondary" period (Division 4) we find 29 per cent. are "positive," and in the "latent period" (Division 6) no less than 35 per cent. are "positive." The "doubtful" cases do not follow this variation.

It is next of interest to tabulate the incidence of a positive Wassermann reaction in the cerebrospinal fluid in the various divisions.

TABLE 2.—INCIDENCE OF A POSITIVE WASSERMANN REACTION IN THE CEREBROSPINAL FLUID

Division	Number of Cases	Number with Positive Wassermann Reaction	Number per Cent. with Positive Wassermann Reaction
1	71	0	0
2	168	1	0
3	107	3	2
4	85	7	8
5	78	5	6
6	115	26	22

It is seen from Table 2 that in Division 1 there was no instance of a positive Wassermann reaction in the cerebrospinal fluid, while in Division 2 there was only one case, which gave a slightly positive result.

To show the relation of the Wassermann reaction in the cerebrospinal fluid to the number of cells present we have prepared the following table (Table 3).

It will be noted from Table 3 that in every instance but one a fluid with 200 cells or over per cubic centimeter gave a positive Wassermann reaction. Also that with one exception the fluids containing from 0 to 9 cells all gave negative reactions. We will quote this exception in detail.

ILLUSTRATIVE CASE

CASE 88.—The patient had been infected in 1907. The original symptoms and treatment were not recorded. On Nov. 9, 1917, the patient was admitted to the hospital because of a positive Wassermann reaction. He had a general adenitis and scars of ulcers on both legs. Between November, 1917, and January, 1918, he received 2.7 gm. of neoarsphenamin. On April 15, 1918, the patient was readmitted with bilateral eighth nerve deafness. The Wassermann reaction was positive in the serum. The cerebrospinal fluid revealed no cells; the Wassermann reaction was ++++.

The occurrence of a positive Wassermann reaction in the fluid, in the absence of cells or with normal cells, is very uncommon and is

TABLE 3.—THE RELATION OF THE POSITIVE WASSERMANN REACTION IN THE CEREBROSPINAL FLUID TO THE NUMBER OF CELLS

Number of Cells in the Cerebrospinal Fluid	Number of Cases with Wassermann Reaction Positive	Degree of Reaction	Number of Cases with Wassermann Reaction Negative
0-9	1	4 - - - (0 cells)	508
10-19	3	4 - - - (12 cells) 4 - - - (14 cells) 4 - - - (18 cells)	36
20-49	4	4 - - - 4 4 0 0 4 - - - 4 - - -	26
50-99	11	4 4 0 0 4 4 0 0 4 0 0 0 3 0 0 0 2 0 0 0 4 - - - 4 4 0 0 4 4 0 0 4 1 0 0 4 4 0 0 4 4 0 0	6
100-149	7	4 4 0 0 4 4 0 0 4 4 0 0 4 4 0 0 4 4 4 0 4 0 0 0 4 4 0 0	3
150-199	4	4 4 0 0 4 4 0 0 4 4 0 0 4 4 0 0	2
200-299	4	4 4 0 0 4 4 4 4 4 - - - 4 0 0 0	0
300-499	2	4 4 0 0 4 4 0 0	1 (476 cells)
500-999	3	4 3 0 0 4 1 0 0 4 - - -	0
1,000-	3	4 4 0 0 4 - - - 4 4 1 0	0

explained by the previous extensive treatment. It is frequently found that after treatment, a cerebrospinal fluid which has had both a pleocytosis and a positive Wassermann reaction, shows improvement — first, by a decrease of cells, and later by an alteration in the Wassermann reaction. It would appear that Case 88 must have had undetected central nervous system disease in November, 1917, that treatment had reduced the cells of the cerebrospinal fluid to normal at the time of the examination in April, 1918, but the Wassermann reaction was still positive. It is quite possible for the eighth nerve deafness to have progressed as the result of damage done before treatment was given, while at the same time the cerebrospinal fluid was progressing toward normal.

PRESENCE OF SPIROCHETES IN CEREBROSPINAL FLUID

In fifteen of the cases with the highest cell counts, we endeavored to find the *Spirocheta pallida* in the cerebrospinal fluid. All the examinations were made within three hours of lumbar puncture. The fluid was centrifuged at high speed for fifteen minutes, then poured out gently leaving a deposit on the bottom of the tube which was taken up by a capillary pipet and examined under a cover slip by dark ground illumination. In only one case was *S. pallida* found, this man having been infected twenty weeks previously and having 1,000 cells in the cerebrospinal fluid.

GENERAL CONSIDERATIONS

In reviewing the results as a whole it is necessary to consider what previous treatment these patients had received. There are two ways in which it might have influenced our findings: (1) By decreasing the number of positive cases, and (2) by increasing them owing to a provocative effect.

To determine to what extent the provocative factor operated we divided our cases into two groups; (1) the untreated, and (2) the recently treated. In the latter group we included only those patients who had received intravenous treatment within fourteen days before they were examined, because this is the most favorable period in which to observe provocative effects when they occur. In the untreated cases we found 15 per cent. with positive pleocytosis and 11 per cent. doubtful; and in the recently treated cases 15 per cent. positive and 12 per cent. doubtful. The percentages in both groups are thus almost identical, and it is quite apparent that there is no obvious provocative pleocytosis from treatment by arsenical preparations given intravenously.

Comparing the group of untreated cases with those patients who had received intravenous treatment previously to fourteen days before examination, we obtained similar results, and may therefore conclude

that any treatment our patients had received before admission did not affect our findings.

THE RESULTS OF THE EXAMINATION OF THE CENTRAL NERVOUS SYSTEM

The patients who had any clinical evidence of central nervous system disease, either signs or symptoms, may be conveniently summarized in the following tabulated form.

TABLE 4.—INCIDENCE OF CENTRAL NERVOUS SYSTEM DISEASE IN EACH DIVISION

Division	Number of Cases with 10 Cells or Over per C.Mm. in Cerebrospinal Fluid	Number of Cases Examined Neurologically	Number of Cases with Clinical Evidence of Disease in Central Nervous System	Number with Signs	Number with Symptoms
1	2	2	0	—	—
2	15	11	0	—	—
3	18	15	1	1	0
4	25	23	7	6	2
5	14	12	5	4	3
6	41	36	10	9	3
Total	115	99	23	20	8

Twenty-two "doubtful" cases were investigated. These included some from each of the six divisions, and in only one case (Division 3) was any abnormality found. This man had occipital headache for nine days and his cerebrospinal fluid contained 8 cells per cubic centimeter. In the examination of the internal ear by testing the bone conduction, Weber's, Rinné's and Swabach's tests were used. In Table 5 a summary of our results is given.

TABLE 5.—SUMMARY OF RESULTS OBTAINED IN THE EXAMINATION OF THE INTERNAL EAR

Division	Number of Cases with 10 Cells or Over per C.Mm. in Cerebrospinal Fluid	Number of Cases Examined for Internal Ear Function	Number of Cases with Internal Ear Function Abnormal	Number of Cases Bone Conduction Diminished		
				Right Side Only	Left Side Only	Both Sides
1	2	2	0	—	—	—
2	15	10	2	0	1	1
3	18	12	4	0	1	3
4	25	19	7	0	0	7
5	4	10	4	0	1	3
6	41	26	13	4	2	7

Nineteen "doubtful" cases were also examined and six were found to be abnormal. Thus, out of a total of ninety-eight cases, thirty-six were found abnormal (36 per cent.).

FURTHER OBSERVATIONS

To determine to what extent this result was due to syphilis we examined in a similar way a series of controls. In fifty nonsyphilitics chosen at random it was found that fifteen had diminished bone conduction, a percentage almost as high as among syphilitics with pleocytosis. In six of these fifteen, gunfire might have been responsible for the abnormality, but in the other nine no sufficient cause was apparent. We also examined fifty syphilitics who had normal cerebrospinal fluids and found that twenty-nine had diminished bone conduction. In thirteen of these gunfire might have caused the defect. We, therefore, in view of the large number of abnormal cases among the controls, are not prepared to attach much importance to diminished bone conduction as indicating syphilitic disease in the central nervous system.

The eye-grounds of fifty-three "positive" cases were examined by Surg.-Lieut. Commander R. J. E. Hanson, ophthalmic surgeon to the hospital. These cases were selected from those having the highest cell counts and represent every division except the first. The following table shows the number of abnormal cases.

TABLE 6.—SUMMARY OF RESULTS OBTAINED IN THE EXAMINATION OF THE EYE-GROUNDS

Division	Number of Cases with 10 Cells or Over per C.Mm. in Cerebrospinal Fluid	Number of Cases Whose Eyes Were Examined	Number of Cases With Abnormal Eyes
1	2	0	—
2	15	3	3
3	18	8	5
4	25	13	9
5	14	7	6
6	41	22	17
Total	..	53	40

No examination of the eyes was made in "doubtful" cases. Surg.-Lieut. Commander Hanson was able to detect very slight but quite definite changes in the eye-grounds, which were considered to be the early stages of the syphilitic retinitis, well known in later stages of the disease. We offer the following notes of this condition written by Surg.-Lieut. Commander Hanson.

"RETINIS EX LUE" (EARLY STAGE)

Typical Signs.—The conditions vary in their intensity but three types of signs in the fundus oculi were noted.

1. Hyperemia: The retinal venules especially were over full.

2. Engorgement: Enlargement and cloudy appearance of the perivascular lymph spaces around the retinal vessels and around the papilla (syphilitic halo).

3. Pigment overgrowth and disturbance in the retina: Small rounded woolly-looking opacities with fine spidery connective tissue changes without apparent upset to the functions of the rods and cones.

In connection with Paragraph 3, it is interesting to recall that there are physical and chemical changes in the cerebrospinal fluid and that this is intimately connected with the subarachnoid contents and these last with the retinal lymph streams. With regard to Paragraph 2, one recalls the extensive pigmentation changes in the skin lesions of the secondary stage.

Summary.—There was little evidence of interference with function, namely, with fields, form sense, light difference, and color thresholds. No alterations in the fundus oculi were observed in the cases seen shortly after the appearance of the inoculation lesions. In the later cases the changes in the fundus oculi were: (1) Symmetrical; (2) mainly peripheral, and (3) diffuse and not circumscribed, that is, not more marked nor intense at one part of the periphery than another. No hyalitis nor choroiditis was observed.

TREATMENT AND ITS RESULTS

Treatment has been confined to the use of arsphenamin preparations given intravenously. We have used neoarsphenamin almost entirely. No mercury has been given. Thus we have made it possible to observe the effect of one drug or one type of drug uninfluenced by the effect of minor therapeutic agents, and although it is at present too early to form any far reaching conclusions on the results of treatment it will be of interest to state what we have already observed.

Whenever possible, patients have been recalled for reexamination or further treatment when this was desirable, and we have been able to make two or more examinations of the cerebrospinal fluid in fifty-four "positive" cases. The details of these cases and the treatment given are shown in Table 7.

DOUBTFUL CASES REEXAMINED

Eight "doubtful" cases (from 5 to 9 cells, inclusive, per millimeter) were reexamined after treatment. Four became quite normal, three remained "doubtful," while one actually showed a "positive" pleocytosis. This case is given in detail:

SUMMARY OF CASE

CASE 1043.—The patient was infected Jan. 28, 1918; he was examined April 17, 1918. He had phimosis, balanitis, subpreputial sores, marked general adenitis, and a papular syphilid. *S. pallida* were present in the penile sores. The Wassermann reaction was positive in the serum. The cerebrospinal fluid contained six lymphocytes per cubic millimeter and gave a negative Wasser-

TABLE 7.—The Details of Cases in Which the Cerebrospinal Fluid Was Reexamined After Treatment.

Case No.	Before Treatment		Treatment between Examinations		Interval (Weeks) between First Treatment and Reexamination	After Treatment		Division of Disease
	No. of Cells	Wassermann Reaction	Dose, Gm.	Preparation		No. of Cells	Wassermann Reaction	
1219	8	0	3.6		6	0	0	Div. 1
1220	7	0	2.55		7	4	0	
897	10	0	2.55		6	0	0	Div. 2
1006	10	0	2.05		12	0	0	
1090	14	0	2.7		12	24	0 0 0 0	
1163	10	0	2.7		5	2	0	
593	740	4 3 0 0	4.5 0.75		5 9	20 2	0 0	Div. 3
771	8	0	2.7		7	4	0	
821	10	0	2.55		14	4	0	
831	10	0	2.7 2.7		8 13	28 12	0 0	
856	50	0	2.55		8	5	0	
1043	6	0	2.7		8	20	0	
1119	22	0	2.7		6	6	0	
1258	36	4 - - -	2.7	Neoarsphenamin	10	0	0	
139	254	4 - - -	2.7		8	14	3 0 0 0	Div. 4
355	8	0	2.7		8	6	0	
548	1,000	4 4 0 0	4.5 2.7		10 23	42 3	0 0	
555	804	4 0 0 0	4.5		6	16	0	
560	834	4 1 0 0	3.45		5	70	0	
732	48	0	2.7		8	2	0	
783	23	0	2.7		7	2	0	
1007	6	0	2.7		8 22	6 2	0 0	
1021	12	0	2.7		9 17	2 9	0 0 0 0 0	
1056	290	4 - - -	2.95 4.8	Galyl	4 10	56 22	4 4 0 0 4 1 0 0	
384	144	4 4 0 0	3.6 1.05		5 14 21	68 20 28	4 4 0 0 - 0 - - 4 0 0 0	Div. 5
607	38	0	2.7 0.75		6 24	10 10	0 0 0 0 0	
726	66	4 4 0 0	2.7		7 12	10 10	4 4 0 0 4 4 0 0	
840	42	0	2.55	Neoarsphenamin	10 24	8 6	0 0 0 0 0	
876	5	0	2.4		6	0	0	
927	16	0	4.45		5	8	0	

TABLE 7.—THE DETAILS OF CASES IN WHICH THE CEREBROSPINAL FLUID WAS REEXAMINED AFTER TREATMENT—*Continued*

Case No.	Before Treatment		Treatment between Examinations		Interval (Weeks) between First Treatment and Reexamination	After Treatment		Division of Disease
	No. of Cells	Wassermann Reaction	Dose, Gm.	Preparation		No. of Cells	Wassermann Reaction	
956	10	0	2.55	Neoarsphenamin	9	12	0	
1274	200	4 4 0 0	2.7		6	28	0	
1278	8	0	2.55		13	8	0	
125	1,500	4 - - -	1.8 and 0.65	Neoarsphenamin	56	18	- - - -	Div. 6
			3.45	Arsphenamin	96	10	4 3 0 0	
276	74	4 4 0 0	2.7		13	15	4 0 0 0	
520	107	4 4 4 0	4.5		7 16	16 10	4 - - - 0	
619	156	4 4 0 0	3.3		19	12	4 0 0 0	
620	128	4 4 0 0	2.25		6	14	0	
627	14	4 - - -	2.7		8 11	2 2	0 0	
664	11	0	2.7		8	2	0	
705	38	4 - - -	2.7		6 25	28 252	0 4 4 0 0	
713	28	- - - -	3.3	Neoarsphenamin	14	6	0	
740	112	4 0 0 0	3.6 1.8		6 14	10 10	3 0 0 0 3 0 0 0	
753	184	0	3.15		11	24	0	
767	132	0	2.7		8	14	4 - - -	
792	380	4 4 4 0	2.7		8	70	4 4 0 0	
957	10	0	2.7		10	4	0	
960	38	4 - - -	2.7		11	16	4 - - -	
1084	170	4 4 - -	2.4		8	26	4 4 4 1	
1137	82	4 4 0 0	2.4		7	6	0	
1141	102	4 4 4 0	4.65		5	28	4 4 0 0	
1164	1,100	4 4 1 0	?		7 10	30 0	4 0 0 0 3 0 0 0	
1177	182	4 4 0 0	2.7		7 13	8 4	4 0 0 0 0 0 0 0	

mann reaction. He had six doses of 0.45 gm. of neosalvarsan at three-day intervals from April 18 to May 7, 1918. On June 13, the serum was negative; the cerebrospinal fluid contained 20 lymphocytes per cubic millimeter and gave a negative Wassermann reaction.

COMMENT

There is therefore evidence to show that the central nervous system may be involved although the Wassermann reaction in the serum is

negative. This might occur in two types of cases. Of the first type — the "nerve-relapse' '— Case 1043 affords an example. Here, treatment had been sufficient to check the progress of the disease throughout most of the body but had left a few active spirochetes in the nervous tissues, and although they were as yet too few to produce a positive Wassermann reaction in the serum, they gave evidence of their activity by a pleocytosis in the cerebrospinal fluid. The second type is the untreated early case of Division 1.

In Table 1 it will be seen that there are two examples with positive pleocytosis and nine with doubtful. These, of course, are simply cases in which pleocytosis indicates involvement of the nervous system before the Wassermann reaction in the serum is expected to be positive. It should not be taken for granted that all the decrease of abnormalities in the cerebrospinal fluid is due solely to the treatment given. The incidence of central nervous system involvement in early cases is so much greater than the later manifestations of nervous diseases, that it must be admitted that many of the early lesions recover more or less spontaneously.

SUMMARY AND CONCLUSIONS

1. In a series of 624 unselected cases of syphilis in all stages of the disease, 18 per cent. had 10 cells or over per cubic centimeter and 12 per cent. had from 5 to 9 cells, inclusive, per cubic centimeter in the cerebrospinal fluid.

2. In 80 per cent. of cases which had abnormal cerebrospinal fluid there was no clinical sign nor symptom of nervous disease, although 29 cases had over 100 cells per cubic centimeter, 9 had over 300 cells per cubic centimeter, and 3 had 1,000 cells or over per cubic centimeter. Many of the other 20 per cent. had symptoms so slight that they were of uncertain value in pointing one to central nervous system involvement.

3. Some cases of pleocytosis occur soon after infection before the Wassermann reaction in the serum becomes positive. The incidence of abnormality increases as the disease progresses. In Division 4 (so-called late secondary period) 29 per cent. had 10 cells or over per cubic centimeter, and 12 per cent. had from 5 to 9 cells per cubic centimeter in the cerebrospinal fluid.

4. In Division 6 (cases having no active signs of syphilis over six months from infection) 35 per cent. had 10 cells or over per cubic centimeter in the cerebrospinal fluid and 12 per cent. had from 5 to 9 cells per cubic centimeter; 22 per cent. of this division had a positive Wassermann reaction in the cerebrospinal fluid.

5. It has been possible to detect slight but definite early changes in the eye-grounds of many of the positive cases in this series.

6. Diminished bone conduction is not a reliable indication of syphilitic disease of the central nervous system.

7. That the changes in the cerebrospinal fluid were due to syphilitic disease of the central nervous system is demonstrated by the increase of cells, mostly lymphocytes but occasionally a few polymorphonuclears, by the presence of a positive Wassermann reaction in the fluid, and by the fact that *S. **pallida*** can be demonstrated in the cerebrospinal fluid.

8. A negative Wassermann reaction in the serum does not in every instance exclude the possibility that there is active syphilitic disease of the central nervous system.

9. Previous treatment has had no effect on the number nor on the severity of the abnormalities in our series.

10. Intravenous treatment with arsenical preparations, during the period of our observations, has restored some patients to normal conditions; in nearly all it has had a beneficial effect, but in a few cases the pathological processes in the central nervous system have not been checked even by repeated courses of treatment.

11. The examination of the cerebrospinal fluid is indicated in every case of syphilis.

Abstracts from Current Literature

VEGETATIVE NEUROLOGY AND ENDOCRINOLOGY

YEARLY REVIEW

WALTER TIMME, NEW YORK

Perhaps the most interesting development in the physiology of the vegetative nervous system in the past few years is the attempt of several Dutch investigators to show the dependence of the muscle tonus on the sympathetic ganglionic chain. De Boer[1] and Dusser de Barenne[2] had apparently shown that section of the abdominal sympathetic chain in decerebrate cats was followed by lack of rigidity in the ipsolateral hind leg muscles of the animal. This diminished tone was evidenced by the limp and lower-hanging affected leg when the animal was held up by the integument of the neck. Also the tail deviated to the more rigid side. Following them, and in opposition, their own countryman Van Rijnberk[3] found that in a majority of animals operated on, their conclusion—namely, that section of the abdominal sympathetic affected decerebrate rigidity, was unwarranted. And now comes Stanley Cobb[4] who likewise denies their conclusions in three negations as follows:

1. Section of the abdominal sympathetic in cats has no effect on decerebrate rigidity.
2. Such section causes no hypotonicity of the hind legs or tail.
3. It causes no changes in the tendon reflexes.

Furthermore, stimulation of the abdominal sympathetic chain causes no tonic contraction of the ipsolateral hind leg. He states that the error made by the Dutch investigators was the banal one of varying the method of holding up the animal by the neck—if a normal animal be held in this way, many variations in hind leg and tail postures can be produced by slight changes in the method of holding. Many elaborate theories have been exploded by just such trivialities in the past, and perhaps this is to be added to them. And yet, from certain unpublished results of experimentation on the dorsal sympathetic chain by the present commentator, it would seem to him that the negative statements of Cobb are too sweeping. The subject will of course go through the regular controversial stages, and some physiological truths will eventually be the outcome.

During the past few years criticism and discussion in the field of neuro-endocrinology has centered to a marked degree about the experiments and conclusions of Cannon on the adrenals and their reactivity to emotional disturbance. This had reached the point early in the current year of giving rise to an editorial in *The Journal of the American Medical Association* based on the experimental work of Stewart and Rogoff,[5] in which practically all Cannon's

1. De Boer: Ztschr. f. Biol. **65**:239, 1915.
2. De Barenne: Pflüger's Archiv. **166**:145, 1916.
3. Van Rijnberk: Arch. nederl. de Physiol. **1**:702, 1917.
4. Cobb: Am. J. Physiol. **46**:478, 1918.
5. Stewart, G. N., and Rogoff, J. M.: Am. J. Physiol. **44**:543, 1917.

contentions regarding especially the mobilization of sugar as a result of fright were denied and the superstructure reared on these contentions was demolished. In order to retain an impartial view of the whole matter one ought carefully to determine for himself whether or not these experiments of Stewart and Rogoff are of such nature as to be, without cavil, all-conclusive, before denying affirmative evidence such as Cannon adduced. It may be remembered that they stated that in their animals the secretion of the adrenals is abolished by removing one adrenal gland and sectioning the nerves of the other. In these operated animals, hyperglycemia was produced as well as in the unoperated controls, showing that the adrenals were not the determining factor of such hyperglycemia. This conclusion is faulty for the premise is probably false—namely, that they have abolished the flow of adrenalin into the blood stream by their method. In the first place, the adrenals are not the only adrenalin sources in the body. Many chromaffin structures are found elsewhere along the course of the large blood vessels especially at their points of confluence, and all enmeshed with sympathetic nerve fibers; under which conditions blood from the adrenal veins might very well be found negative to adrenalin presence, albeit present in some measurable concentration elsewhere in the vicinity of these other centers of chromaffin supply; and, secondly, direct pressure on the adrenal bodies by deep diaphragmatic breathing or other pressure will release adrenalin notwithstanding splanchnic nerve section. So that these two sources of adrenalin must be eliminated before Stewart's and Rogoff's conclusion is justified. To blast Cannon's theories on such inconclusive evidence seems unwarranted.

The effect on the blood vessels of *adrenalin* administered hypodermatically had been accepted more or less universally as being constrictive in all groups and systems excepting the pulmonary, cerebrospinal and the coronary. These results were more or less true when large amounts of adrenalin were used. And yet such amounts are probably never secreted by the suprarenals. Small quantities almost invariably produce a vasodilatation.[6] This is a fact largely ignored in spite of the cumulative evidence in its favor. The differential effects produced by adrenalin on cats and dogs is summarized briefly by Hartman[7] as follows: Dilation in skeletal muscle and intestine (small dose), kidney, bone, thyroid and spleen. With small doses the vessels in skeletal muscle more than counteract the constriction in skin and viscera, and a fall in blood pressure results. When the amount of adrenalin is sufficiently large, the constriction of skin and visceral vessels (excepting intestinal) becomes great enough to more than compensate for the dilatation in skeletal muscle, thus producing a rise in blood pressure.

Interest in the thyroid gland is much enhanced, if this were possible, by the isolation in crystalline form of a thyroid hormone by E. C. Kendall of the Mayo Foundation. And not only has the hormone been analytically obtained, but in the past year is said to have been synthetized as well by one of Kendall's assistants. This substance has been called by Kendall, "thyroxin." Its administration in doses as small as a milligram (per day) is followed, in cases of myxedema, by the same curative reaction as follows the use of whole thyroid gland. It has been stated by Plummer, who has given much time to

6. Cannon and Lyman: The Depressor Effect of Adrenalin on Arterial Pressure, Am. J. Physiol. **31**:376, 1913; Hartman: The Differential Effects of Adrenin on Splanchnic and Peripheral Arteries, Am. J. Physiol. **38**:438, 1915.

7. Hartman: Endocrinology **2**:123, 1918.

studying the effects of this active principle, that 10 mg. of thyroxin increase the basic metabolic rate in myxedema 30 per cent. This seems to be the key to the effect of the thyroid hormone in the physiologic activity of the body.

Kendall's method of obtaining thyroxin may be briefly stated as follows: The thyroid proteins are broken into simpler constituents by alkaline alcoholic hydrolysis. These may be separated into two groups as the basis of their solubility in acids, which groups be designated as A and B, respectively insoluble and soluble. The Group A compounds are further separated by continued hydrolysis and the iodin-containing compound isolated in pure crystalline form, with a constant iodin content of 60 per cent. The A iodin compound is "thyroxin." The B compound produces no toxic effects though it seems to possess physiologic properties in certain conditions of the skin.

Starting from the premise that hyperplasia of the anterior lobe of the pituitary body is associated with giantism and acromegaly, T. Brailsford Robertson, then of the University of California, in his experimental studies on growth, especially on the growth of carcinomas in rats as influenced by the secretion of anterior lobe of the pituitary gland, was finally enabled to isolate from the anterior lobe an extract named by him "tethelin" which seemingly resembled the growth factor present in the anterior lobe of the pituitary in all its bearings.

Tethelin is a lipoid, readily hydrolyzed by alkalies, and hence probably partially decomposed by intestinal alkaline juices when administered by mouth. However, it is not totally wasted by such procedure for growth effects are obtained in young mice even when given this way. As it is free from protein contamination, and is soluble to the extent of 5 per cent. in water it may be used for a variety of experimental purposes to which the anterior lobe extract does not readily lend itself. As to its therapeutic properties, it was found that the animals fed with it, had exceptionally good coats, with smooth hair, both abundant and glossy, at an age when normal animals have already begun to lose their hair and whose coats are rough and shaggy. These effects are similar to the hypertrophy of the epidermis and hypertrichosis seen in acromegaly. Taken in connection with the stimulative action of tethelin on carcinomas, it would seem that tethelin is a specific stimulant of epithelial growth. Tethelin is soluble in alcohol and ether, contains phosphorus and nitrogen in the ratio of 1:4 and is precipitated from alcoholic solution by admixture of a definite proportion of ether. As so peculiar a substance was found present in relatively large amounts in anterior lobe extracts, it necessarily fell under suspicion of being the active agent, and the effects of administration amply confirmed this suspicion.[8]

The muscular dystrophies seem to be fairly included now in the domain of the internal secretive disorders. Two groups of observers, taking up the clinical and metabolic aspects of these disorders, have arrived at this conclusion. By virtue of the extreme frequency of pineal shadows seen in adolescence in these cases of dystrophy, coupled with a high percentage of antecedent glandular disturbances in the ancestors and collaterals, together with the resemblance seen in the early symptomatology of pineal neoplasms and muscular dystrophy, Timme[9] postulates a relationship between dystrophy and

8. Robertson, T. Brailsford: J. Biol. Chem., **24**:397, 1916.
9. Timme: Arch. Int. Med., **19**:79 (January), 1917.

the endocrine system notably the pineal body. He examined five members of one family in whom the disease was familial for four generations and found pineal shadows in four of the five.

From the metabolic viewpoint[10] it has been shown that the biochemical

10. Janney, Goodhart and Isaacson: Arch. Int. Med., **21**:188 (February), 1918.

reactions in cases of progressive muscular dystrophy give results resembling those obtained in many hypo-endocrine disturbances; namely, a decrease of preformed creatinin in the urine; abnormal presence of creatin in the urine; low creatinin values in the blood; a normal amount of creatin in the blood; hypoglycemia and delayed glucose utilization. MacCrudden had a year earlier demonstrated the lowered blood sugar content in the blood of a case of progressive muscular dystrophy, and treatment based on such findings has given him some result.

SUGGESTIONS FOR A SCHEME OF GRAPHIC REPRESENTATION OF PERSONALITY AND PSYCHOSIS. H. Douglas Singer, M.D., J. Abnorm. Psychol. **12**: No. 2, pp. 114-130.

It is quite evident that the importance of the relationship of personality and psychosis is getting more and more appreciated. This forms a part of the general tendency which is fortunately coming into psychiatry, perhaps especially in this country, toward a dynamic view of, especially, the constitutional psychoses. This study of Singer aims at systematizing our knowledge regarding personality and psychosis, so that the facts can be put into sufficiently concise form for grasping them and for making generalizations. This is especially important for the functional neuroses and psychoses. Singer is fully aware that all such schemes are as yet tentative. He endeavors to represent the personality traits and the symptoms graphically, by putting them in parallel columns—one side for the traits of endowment, the other side for the psychotic symptoms. Among the former he begins with energy, under which he takes up the vigor of reactions; then the mood; then intellectual endowment. The modes of adjustment are next considered. Here we first have what he calls the primitive or sensual, that is, an entirely frank gratification of desires. Singer says that the questions considered under this heading seem sufficiently obvious to require no special discussion here, but one would have liked nevertheless if Singer had been more explicit. A useful grouping is, however, his division into helpful, harmless and harmful substitutions. The helpful substitutions are those of a domestic, social, practical, artistic sort, the test, wisely, being whether they lead to real accomplishment or activity in the field selected. Harmless substitutions are those which represent a certain outlet of energy but which represent no social gain, such as hobbies. Finally, the harmful substitutions are those which do not accomplish anything and which, moreover, bring the individual into more or less conflict with the environment. Here we find irritability (defined as a substitution of aimless activity for a frank and purposeful method); overscrupulousness (indecision with futile worrying and a tendency to great exactitude in detail); explosive effects such as tantrums; transient enthusiasms; religious fervors; hypochondria (a failure to face actual situations, while an explanation of bodily incapacity is substituted). The next heading is drug addiction. Then comes suspiciousness (a translation of failures into interference by others, etc., which so alter the facts of the situation as to render adjustment to the real facts more or less impossible). Then follows bashfulness, superstitiousness (the tendency to ascribe personal failures to unknown influences). Finally

day-dreaming is taken up (a tendency to seek the gratification of desires by imagining the end as accomplished), and mannerisms.

For the sake of brevity the correlative psychotic symptoms cannot be entered on. Some charts illustrate the method. A chart of manic excitement shows the predominance of frank features; the opposite is seen in dementia praecox. Interesting is the fact that an analysis of a paranoid reaction shows some features similar to dementia praecox (though not the more marked shut-in traits) but with strikingly better energy endowment.

There is no doubt in the mind of the reviewer that the method is a fruitful one for study as well as for teaching purposes.

HOCH, Santa Barbara, Calif.

THE TREATMENT OF GENERAL PARESIS. CLARENCE A. NEYMANN, M.D., and NATHANIEL H. BRUSH, M.D., Arch. Int. Med. **22**:245 (August), 1918.

At present there are several forms of therapy. The so-called mixed treatment—mercury and potassium iodid—may be discarded as used alone. That it is a valuable aid to other forms of therapy there can be no doubt. Next to this in simplicity is the intravenous treatment. Certain cases may be benefited by intravenous use of arsphenamin or its substitutes but there is always the danger of hypertherapy. The resistance of the choroid plexus and the meningeal blood vessels to chemical compounds of complex molecular structure has been demonstrated. Intraspinal therapy with arsphenaminized serum is undoubtedly useful, but the same objections may apply here that characterize the intravenous method. If arsphenaminized serum is given every seven days, great care must be taken to avoid bladder, rectal and other root disturbances. A patient may react well to the first five or six treatments and have subjective or objective bladder disturbances with the seventh. More or less permanent motor root disturbances as well as perineal and sacral anesthesias and paresthesias have been observed after the intraspinal administration of arsphenaminized serum.

The reactions obtained with mercurialized serum (prepared according to the Byrnes method) are entirely different. Immediate reactions are more severe but permanent injury to the muscular or sensory innervation is not observed. This method alone has not given the best results. High dosage is often resorted to in the attempt to check the process. Several reactions will be met, such as high temperature, extreme pain, meningismus, nausea, etc., due to the enormous amount of irritation. The intraventricular treatment and the intradural methods merit consideration. It has been shown that the flow of spinal fluid is toward the foramen of Magendie starting from the ventricles and from the spinal canal. Based on this fact such a therapy is most rational. Dread of necessary surgical procedure prevents most patients from taking advantage of such a method.

The treatment outlined by the authors is, in fact, more or less of a combination of the aforementioned methods.

After the diagnosis is established, the patient is put on a routine course of mercurial inunctions and potassium iodid by mouth. Careful attention is paid to mouth hygiene during the entire period of the treatment. These inunctions are given six days a week and a hot bath on the seventh day; also a saturated solution of potassium iodid is given beginning with 15 drops three times a day, and increasing 1 drop a day until the maximum of 150 drops a day is reached. Usually furunculosis is noticed before this time, thereupon the iodid is discontinued for about a week, to be later recommenced at 15 drops three times a day.

Arsphenamin is given intravenously, beginning with 0.2 or 0.3 gm., according to the body weight of the patient. If the patient reacts badly to this initial dose, all treatment is discontinued and no further attempt is made to treat him. They consider as serious reactions any signs of arsenical rash, neuritis, albuminuria, and marked circulatory disturbances—that is, syncopal attacks.

The next week the patient is given 0.5 or 0.6 gm. of arsphenamin. At the completion of the arsphenamin administration, 50 c.c. of blood are withdrawn into a sterile centrifuge tube, a lumbar puncture is made and the spinal canal is drained.

Investigators are of the opinion that this procedure partly overcomes the aforementioned resistance of the choroid plexus and meningeal vessels to the drug. It is marvelous how much fluid one can withdraw from the spinal canal of a paretic without causing the slightest discomfort; in fact, the more fluid withdrawn, the less reaction is likely to result. The authors have withdrawn as much as 80 c.c. at a time.

The next day the blood, which has been allowed to clot in the icebox overnight, is centrifuged, poured into a second sterile centrifuge tube, again centrifuged and inactivated in a water-bath at 56 C. for half an hour. This overcomes the use of pipets, which, even when plugged with cotton, always involve the danger of salivary contamination.

The third week $\frac{1}{100}$ grain of mercury (Mulford's mercurialized serum) is given intraspinally. Though it is known that animals can be sensitized to foreign protein by intraspinal injections, anaphylactic reactions following the use of this particular preparation have not been observed.

The fourth week, arsphenamin and arsphenaminized serum are again given as described.

The fifth week $\frac{1}{80}$ grain of mercury is introduced in the spinal canal, provided the patient has theretofore shown no unfavorable reaction after the initial dose. From now on the alternate treatment with arsphenamin and mercury intraspinally proceeds regularly. Whenever a patient begins to evince signs of debility, it is best to give him a complete rest and discontinue all treatment.

Twenty-four cases were so treated. Based on results they can be divided into four groups of six patients each. The patients of the first group are all doing well, and with the exception of one have been discharged from the hospital and are at work. The serologic findings of the spinal fluids of five are practically negative. It is possible to change the serologic findings of most patients after this intensive treatment. They may not be permanent. The cell count is the easiest to reduce. Repeated spinal punctures will do so. At least eight intraspinal treatments must have been given before any change is noted in the spinal fluid Wassermann test; often it takes from fifteen to twenty injections. In successfully treated cases traces of the syphilitic amboceptor may be found. The gold curve is changed only after a maximum number of doses have been given. It is not usual for the gold curve to revert to a completely negative reaction. The average duration of the present status of this first group is fifteen months. These are considered as arrested cases.

The second group of six is less satisfactory although somewhat improved. Four of this group resumed their occupations while two are continuing their treatment. This group show some serologic improvement.

The third group showed no clinical or serologic improvement. The last six were harmed by the treatment—one developed a paraplegia; two became incontinent; one died of acute arsenical poisoning, and one developed an arsenic neuritis; finally, one died in convulsions possibly as the result of treatment.

The points in the treatment to be emphasized are (1) long-continued intensive methods as indicated, and early diagnosis; (2) careful use of all arsenic preparations, as the danger of motor and sensory root disturbances cannot be entirely avoided.

There is scarcely a single psychotic manifestation which cannot be simulated by general paresis. Serologic findings may prove a case to be one of general paresis when neurologic and physical findings are not at all characteristic. Complaints may be mostly neurasthenic and hypochondriacal. Importance should be attached to these subjective feelings and to minor neurologic conditions. Often friends or the family may furnish evidence of slight and gradual retrogression. These facts coupled with the laboratory findings may aid in determining the diagnosis. A positive Wasserman reaction in the blood and spinal fluid, a paretic gold curve, a high cell count, and positive globulin tests in a case that shows any mental symptoms whatever may be classed as one of incipient paresis. It is interesting to note that, in a large series of paretic patients examined by the authors, 23 per cent. showed a negative blood Wassermann reaction.

The results obtained by Neymann and Brush considering the types of patients dealt with were excellent, and show the value of coordinated clinical and laboratory work.

WEISENBURG, Philadelphia.

WAR PSYCHOSES: A report of six unusual cases showing memory disorder. TEMP. CAPT. D. K. HENDERSON, M.D., Rev. Neurol. & Psychiat. May and June, 1918.

The author has described six cases of very unusual war psychoses. All of them fit more or less into the Korsakow syndrome, showing extraordinary memory defect, confabulation and an absence of retention for recent events. The first three showed this mental picture, following burial. Of the other three, one followed dysentery, one enteritis, one dysentery plus malaria. These last three are good examples of toxic-exhaustive states and showed a more or less typical Korsakow syndrome; thus the picture is not unlike that encountered in civil life. The first three cases are much more unusual and would probably best be considered as examples of what Mott has termed "commotio cerebri," and the condition in each may possibly have been accentuated by the inhalation of noxious gases.

However, all six cases have much in common as far as the mental history is concerned. It is not by any means unusual to see cases with amnesia for the period of burial, often lasting hours or days afterward; but it is exceedingly uncommon to see cases showing the peculiar confabulatory state described.

The close association between cause and effect, the patients developing their peculiar mental state directly after the accident, would seem to put the hypothesis of mental shock out of the count. Furthermore, all of these three cases, up until the accident occurred, had been able to "carry on" as formerly. Further, the mental picture exhibited by each was much more in the nature of an organic than of a functional type of reaction.

The observations of the author seem timely. After Mott's first description of minute hemorrhages into the brain and the assumption of an organic basis for many cases of so-called "shell-shock" a justifiable reaction among the psychiatrists took place. Many so-called organic cases proved to be functional. It is therefore of great interest to note these three cases, undoubtedly on an organic basis.

NEYMANN, Baltimore.

CONDUCTION IN PERIPHERAL NERVE AND IN THE CENTRAL NERVOUS SYSTEM. E. D. Adrian, M.B., M.R.C.P., Brain, Lond., **41:** Part I, 23-47, 1918.

The paper is largely a summary of the work of Keith Lucas on the conduction of the nervous impulses considered from the neurologic standpoint. When the frog's sciatic nerve is stimulated mechanically, electrically or chemically the gastrocnemius muscle contracts after a short, appreciable interval. The stimulus sets up some disturbance in the nerve, which travels down it at the rate of 28 meters a second. The nature of this nervous impulse is unknown and only the electrical response which accompanies it can be detected. It has been found that the stimuli must be separated from one another by more than 0.003 second or the subsequent stimulus will fail to set up the nervous impulse. If the stimuli are repeated with sufficient rapidity the number of nervous impulses may be only a fraction of the number of stimuli. The activity of the nerve fiber, therefore, is not continuous, and conduction proceeds by means of a series of discrete impulses which cannot follow one another at less than a certain interval. This interval is known as the refractory period. There is an all or none relation between the strength of the stimulus and the contraction of the muscle fiber, as shown by experiments with preparations containing very few nerve and muscle fibers.

The intensity of the nervous impulse can be measured in terms of its ability to travel through regions of decrement produced by narcotizing varying lengths of nerve fiber with varying intensity. It is thus found that the intensity of the impulse does not vary with the strength of the stimulus, that stronger stimuli have no advantage. An impulse reduced in intensity recovers again when it passes out of the region of decrement into normal fiber. In a normal fiber, therefore, the intensity of the impulse at any point depends only on the local condition of the fiber at that point. Recovery after the passage of the impulse may be divided into three stages.

1. The absolutely refractory period when all activity is abolished.

2. The period of depressed activity, in which the nerve conducts an impulse of small intensity and needs a very strong current to offset it.

3. The period of enhanced activity, when the excitability is greater than the normal and the intensity of the impulse is also greater.

Central conduction differs from peripheral mainly in the greater susceptibility to fatigue of the synapses and in the property which enables a single impulse in the afferent nerve to set up a series of impulses in the efferent, so that the response may outlast the stimulus by several seconds. We may suppose the central nervous system to consist of a number of neurons communicating with one another by junctional areas or synapses. The synaptic areas are regions of imperfect conduction; the impulse suffers a decrement as it passes through them. The duration of the refractory period and the extent of the change which occurs in the period of enhanced activity may vary and may have different values in different synapses or different parts of the same synapse. At some point in the synaptic region the passage of a single impulse may initiate a succession of impulses, and at another conduction is possible in one direction only.

Whatever our conception of the central nervous system may be, there can be little doubt that the amount of energy leaving it by afferent nerves may be considerably greater than the amount entering it as a result of an external stimulus. Wherever afferent nerves branch repeatedly there is a possibility of turning one impulse into two, the increased energy being supplied locally by the fibers themselves.

If the central nervous system contains regions of decrement there should be no difficulty in accounting for at least one form of inhibition and summation analogous to that encountered in the peripheral nerves. In view of the complications introduced in the central nervous system where the impulse has to pass through several relays of conductors and junctional regions with different rates of recovery the most varied possibilities are opened up without introducing any assumptions that have not been proved in the case of peripheral conduction.

If we grant that the synaptic regions may have different rates of recovery there is no difficulty in explaining the fact that stimulation of an afferent nerve may lead to contraction of one muscle and inhibition of its antagonist. We must suppose that the frequency of the impulses reaching the final common path of the inhibited muscle is so great that all the impulses are of subnormal intensity and are therefore extinguished before they reach the muscle. The frequency of the impulses reaching the muscle which contracts must be slower, so that the impulses shall be large enough to pass. These conditions will be realized if at some point on the path leading to the muscle which contracts there is a region which recovers so slowly that every other impulse from the afferent nerve arrives during the absolute refractory period and is extinguished completely. The effect of this will be to halve the number of impulses passing toward the muscle, so that each will be large enough to avoid extinction; in the other path, where the impulses do not pass through a region of slow recovery, the frequency will be great enough to cause inhibition.

Most of the phenomena of reciprocal innervation may be accounted for by a mechanism of this type. However, difficulties begin to arise when we come to consider the balanced effects of inhibitory and excitatory stimuli.

The suggested mechanism of central conduction may prove to be absent or present only in a small degree. However, the hypothesis has the advantage that it does not demand any properties in central conduction which cannot be shown to exist in some degree in simple conducting tissues.

REYE, Detroit.

THE EAR IN STUNT FLYING. MAJOR LEWIS FISHER, M.C., and CAPT. HARRY LYMAN, M.C., J. A. M. A., **71**:1977 (December), 1918.

Neurology has always fostered the careful study of the relation of special-sense-mechanisms to the central nervous system. Because of the elaborate and intimate connection of the ear with the nervous system a study of the ear-mechanism has opened up a peculiarly attractive and promising field of investigation to the neurologist and otologist. During the past several years many investigators have made clinical contributions in the application of these studies to the problems presented in cases of vertigo, syphilis of the central nervous system and intracranial localization.

In the past two years aviation, as an important factor in the war, brought with it many new medical problems which have proved to be largely neurologic. Among these were numerous neuro-otologic problems—the paper of Major Lewis Fisher and Capt. Harry Lyman being of peculiar interest. The article emphasizes the following points:

1. That crashes during stunt-flying result as a rule from something having gone wrong with the pilot rather than with the machine—that errors of judgment, carelessness, etc., do not adequately explain these accidents—that many pilots who survive such crashes speak of having been affected by a momentary loss of faculties due to an over-powering dizziness.

2. The realization that during stunt-flying the pilot is whirled violently in space, and a knowledge that the ear is the chief organ affected by whirling, naturally directed the attention to the study of the ear-mechanism.

3. Whirling experiments conducted on experienced aviators have shown conclusively that the various aerial evolutions, or "stunts," can be exactly imitated or reproduced by whirling them in a laboratory apparatus—that by whirling them in a certain way the aviators would feel as though they were in a "spinning nose-dive" and that whirling them in another direction they would feel as though they were doing a "tight spiral," etc.

4. The facts gleaned by these experiments were in absolute accord with well known otologic principles and the knowledge of the ear as a motion-sensing organ, and demonstrate conclusively that stunt-flying is essentially an ear problem.

5. The otologic facts and principles referred to were: (*a*) Each inner ear in addition to the cochlea, or the hearing portion, consists of a common chamber from which project three semicircular canals at right angles to each other—the entire system containing fluid. Because of this arrangement no change of position is possible without producing some movement of fluid in one or more of the canals. Movement of fluid in these canals stimulates nerve-endings and results in certain messages to the brain which are there interpreted as body movement. Therefore, the ear constitutes one of the motion-sensing organs of the body. (*b*) When an individual is whirled—be it in the laboratory or in an aeroplane—there is produced a movement of fluid in certain definite canals and planes. If the turning be suddenly altered or stopped, or the aeroplane comes out of a rotating maneuver, the fluid in the canals continues to move in its former plane by sheer force of momentum. This circulation of the fluid (by momentum) is interpreted by the individual as body movement, but not being in accordance with fact, the body having ceased to revolve, constitutes vertigo or dizziness, and is disturbing to the individual. Labyrinthine vertigo, therefore, is a false sensation of motion similar to the visual illusion of motion observed when watching a moving train from the window of a stationary coach, both being unavoidable phenomena of normal special sense mechanisms which, however, the subject easily learns to interpret and disregard.

The authors warn those who are prone to draw hasty conclusions not to be misled into thinking that individuals in whom the labyrinths have been destroyed, congenitally or through disease, would be peculiarly adapted as aviators because of the immunity from vertigo which they would enjoy as a result of a lack of a normal ear-function. The importance of the ear-mechanism as a motion-perceiving apparatus is of such overwhelming usefulness to an individual traveling in a fluid (air) medium that the advantage derived from a vertigo immunity is as nil compared with the benefits derived from the former. This is particularly evident to those who have seen how deaf-mutes are completely lost when taken up in an aeroplane and are absolutely unable to detect the direction of movement the moment they close their eyes. Furthermore, normal individuals can acquire vertigo immunity without much difficulty in a short time.

The various "stunts" or air maneuvers are then analyzed from an otologic standpoint. Thus, for instance, in the so-called spinning nose-dive in which the aviator, face downward, is whirled about an axis with head and body practically parallel to the ground, there is a stimulation in the vertical semicircular canals in a frontal plane. When he comes out of the spin the plane of vertigo, which until now has been parallel to the ground or horizontal,

becomes vertical in a frontal plane, so that instead of feeling that he is whirling horizontally, he feels himself whirling in an up and down plane. This being very disturbing he is apt to lose himself momentarily, and in attempting to correct for this illusionary movement, to throw himself into another spinning nose-dive in the opposite direction. The identical condition can be simulated in the turning chair. When he is whirled with his head forward it simulates his position during the spinning dive. When he attempts to sit up after the turning, he similarly changes the horizontal vertigo with which he started into a sensation of whirling in a vertical plane. Here, too, he attempts to correct the false impression and in doing so he throws himself to one side or the other so markedly, that unless caught by the examiner he falls to the floor. The obvious remedy in both instances is to keep the head down in the original position so that the vertigo always remains in a horizontal plane.

Experienced fliers are not upset by the vertigo induced during stunting for the reason that continuous practice in the air and many repetitions have taught them to properly interpret the confusing subjective sensations, so that they learn to disregard them. Some fliers also assume instinctively those positions of the head which tend to keep the plane of vertigo horizontal at all times, in this way minimizing any disabling effects induced.

The usefulness of the knowledge that stunting is an ear-problem is twofold: (1) The flier may be taught to assume certain positions of the head during or following certain stunts, and in this way minimize any disturbing effects, and (2) the flier may acquire safely a vertigo tolerance or education in a laboratory apparatus instead of in an aeroplane among the clouds. This is accomplished by the orientator, a mechanical apparatus so constructed that any evolution in an aeroplane, except actual forward progression, such as the "loop," "barrel-roll," "Immelmann turn," "the spinning nose-dive," "ascending and descending spirals," "the wing-over," etc., can be successfully reproduced in the machine.

JONES, Philadelphia.

A CASE OF CHILDHOOD CONFLICTS WITH PROMINENT REFERENCE TO THE URINARY SYSTEM; WITH SOME GENERAL CONSIDERATIONS ON URINARY SYMPTOMS IN THE PSYCHONEUROSES AND PSYCHOSES. C. MACFIE CAMPBELL, M.D., Psychoanal. Rev. **5**: No. 3, pp. 269-290.

This is an interesting study of a child observed at the dispensary from the age of 7 to 11. She was boisterous, inattentive, bizarre in her behavior, and presented some very definite trends, namely, obsessive questioning, a tendency to bed-wetting and wetting herself in the day time, together with deliberate retention of urine, intense interest in plumbing (questioning about water pipes, sewers, even attempt to get down into the sewer), frequent questioning also about urine, where it comes from, where it goes. She also had a tendency to exhibitionism at home and in the doctor's presence. A certain coquettishness and a constant desire to be examined physically by the physician, were also present. The patient was not analyzed and not questioned. Finally, she spontaneously gave naively direct expression to pleasurable sensations associated with urination and with fulness of the bladder, also to

her sexual interests in her little brother's genitals and to sexual playing with him—all of which, without any special interpretation, put into a clear light the reasons for her peculiar behavior before.

Campbell calls attention to a case of Havelock Ellis in whom also direct expression was found of pleasurable sensations connected with the act of urination and with a full bladder. He reports some neuroses in which, in view of these findings, it would seem that those positive pleasures, in addition to other motives (in the cases particularly the desire to shirk marital relationship) may account for retention of urine and frequent urination. The relationship of the sexual instinct with urination is often seen in schizophrenia, and he mentions a case in which the act of drinking urine was frankly associated by the patient with the sexual act. In general, the pleasurable nature of the urinary activity frankly admitted by this little girl, Campbell says, throws light on all sorts of urinary symptoms in childhood, as well as similar symptoms in psychoses and neuroses; it shows the possible relationship of symptoms referable to urinary activity with the sexual instinct, and it also throws light on obsessive questioning in children (interpreted as due to an interest which was not allowed direct expression), on peculiar interests (here in plumbing, etc.), peculiar attitudes, and the like. Moreover, "such an experience with a child of poor nervous endowment may sensitize us to minor manifestations of similar conflicts in the life of the ordinary child."

HOCH, Santa Barbara, Calif.

WAR PSYCHOSES: Amnesia as a Defense Mechanism for Desertion. TEMP. CAPT. D. K. HENDERSON, M.D., Rev. Neurol & Psychiat. May and June, 1918.

The author gives a careful and exhaustive study of fourteen cases of amnesia examined by him. All these were men in the military service, who had left the lines or their camp, were arrested as deserters, and claimed a loss of memory for the whole period of their wandering. In some cases these fugue-like spells may seem to be synonymous with flight or desertion, while in others they can be traced back to fairly definite factors.

The cases naturally fall into three large groups: (1) those organically determined, for example, head trauma, general paralysis, mental deficiency, epilepsy, toxic-exhaustive states; (2) those associated with well-recognized forms of the psychoneuroses or of functional types of mental disturbance, for example, manic-depressive insanity, dementia praecox, and (3) those who had never shown any previous special psychotic symptoms but who later were shown to have developed the amnesia on the basis of complex factors. It is, of course, this latter group which gives rise to a great deal of difficulty, and in which the question of responsibility, or lack of it, comes acutely to the fore-front.

Six of the fourteen cases described in detail by the author fall into the first group. Two are examples of recurrent amnesia after severe head traumas, in patients who had been sick before entering the service. In one the amnesia was due to general paresis, and in another the main etiologic factor was undoubtedly overindulgence in alcohol. This had seriously undermined his constitution and had caused such a general mental reduction that the patient really had become irresponsible for his action. The other two cases are good

examples of wandering fugue-like states with amnesia in mental defectives. The mental defective has great difficulty in adapting himself to the ordinary stress and strain of military life, and under shell fire he very easily becomes befuddled and in consequence is apt to wander away from his unit.

These two cases of mental defect are good examples of many such. The patients, by their foolish actions, are very apt to be a source of danger to all associated with them, and should be rigidly excluded from the army, or at least from active service. They, of course, cannot be held responsible for any of their foolhardy and foolish acts.

The next four cases fall into the second group. Two had a psychoneurotic make-up; one had a hallucinatory paranoid trend before entering the service; one gradually developed a mental disturbance while in the service. The mental disturbance of this last patient seems to have been caused entirely by the stress and strain of active service. His resistance became lowered, an amnesia developed, no doubt as a defensive measure, and his latent trends asserted themselves.

In the last four cases belonging to the third group, the amnesia came, more or less, out of a clear sky, and was the first indication that anything was seriously wrong with the patient. It is extremely difficult to determine how far these patients were conscious of and should be held responsible for their acts.

In the cases belonging to the organically determined and to the functional nervous and mental disorder groups it has usually been easy enough, by means of a careful history, to make sure that the individual in question was unstable, and at the time the amnesia took place was nervously or mentally affected. Particularly in the cases of general paralysis and mental deficiency, it will be readily admitted that the mental disorder is such that any person so suffering could not be held responsible for his acts. In the other cases belonging to these two groups—for example, the cases with head injury, alcoholism, psychoneuroses, and schizophrenia—it is a difficult problem to decide how much weight in the production of the amnesia should be given to the head injury, to the alcoholism, and to the various types of mental disorder exhibited, and how much emphasis should be laid on the psychological factors which were also present.

In all the groups the amnesia has been a defense reaction toward a situation which could not be met in a healthy, aggressive way. In the cases belonging to the first two groups this reaction has taken place at a more or less unconscious level; while as regards the last group, it has taken place at a more or less conscious level. How far the patients of the last group should be held responsible for their acts is open to fair argument.

NEYMANN, Baltimore.

OBSERVATIONS ON TWO HUNDRED AND FIFTY CASES OF GUNSHOT WOUNDS OF THE PERIPHERAL NERVES. MAJOR C. NOON, R.A.M.C., J. Roy. Army Med. Corps, London, **31**:39, 1918.

Although the conclusions of the author are somewhat platitudinous, such as, "Successful recovery depends on early, correct and continuous treatment," he has had the opportunity of examining 250 cases of this kind of injury and has operated on 102 of them. He divides the clinical phenomena into four syndromes:

1. The syndrome of complete division of the nerve trunk is characterized by complete paralysis in the muscles supplied by the divided nerve, loss of both protopathic and epicritic sensibility, pallor and coldness in the part affected, diminution in the subcutaneous fat, a dry skin and frequently ulceration of the skin.

2. The syndrome of compression often follows, in the form of a relapse, after an early improvement. These cases are the most numerous and the most favorable for operative treatment. The motor paralysis is less marked than when the nerve has been divided and the trophic lesions do not occur, but there is a form of sensory dissociation in that the area of loss of sensibility to pain, as tested by the pin prick, is greater than that in which there is loss of sensation to light touch.

3. The syndrome of incomplete lesion with irritation shows an incomplete paralysis accompanied by neuralgic pains in the part. The skin is glossy and a mottled red, and tender to stimuli. There is generally a profuse sweating over the part affected, and the sweat is strongly acid and bad smelling.

4. The syndrome of interruption, followed by restoration of function, is shown by a loss of sensation and motor power but little, if any, wasting. These cases usually recover completely in about three months, and an operation is not required. The nerve is probably not directly injured but suffers from concussion.

An operation is urgently needed in the case of a divided nerve, and the ends of the nerve should be brought together and united as soon as possible. Even when there is a considerable gap between the ends of divided nerves they can usually be brought together, if the operation wound is large enough to permit a considerable portion of the nerve to be exposed; for instance, in operating on the ulnar nerve in the forearm the incision should be from just below the elbow down to the wrist. The nerve should first be freed above and below the injury and dissected out carefully; often it will be found that there is a bridge of fibrous tissue joining the two ends of the nerve and, before this is divided, a fine silk suture should be passed vertically through each end. This is of great value in retaining the proper orientation of the ends of the nerve so as to join together the corresponding nerve bundles. If the nerve, after suture, can be placed in a bed of healthy tissue it is not necessary to surround it with any foreign tissue, but if there is much scar tissue present the author prefers to suture the nerve loosely in a bed of fat cut from the patients own thigh. A very important point is that the limb should be so bandaged that there is a minimum of tension on the nerve.

Electricity, massage and passive movements are of great value in the after-treatment, and the cases may continue to improve even after two or three years. Electrical treatment should be continued for at least six months after an operation.

The ulnar nerve was the one most frequently injured; the median, musculospiral and external popliteal followed in the order mentioned.

CAMP, Ann Arbor, Mich.

PALLIATIVE TREPHINING IN CASES OF TUMOR OF THE INFUNDIBULAR REGION. S. P. KRAMER, M.D., J. Nerv. & Ment. Dis. **48**:353 (November), 1918.

Kramer reports four cases of tumor of the hypophysis in which pressure symptoms were relieved by palliative operations, namely, by turning back a large frontal flap and freely incising the dura, then folding the bone flap back and suturing the skin.

Kramer deplores the use of the word "decompression" as furthering the idea that relief of increase of intracranial pressure may be produced by operation on any part of the skull—with which he entirely disagrees. He insists that the purpose of palliative operations is to relieve pressure in the nerves of the base of the brain—particularly on the optic nerves—and believes that the frontal bone method is the most favorable sight for this operation.

WEISENBURG, Philadelphia.

SOME EXPERIMENTS BEARING ON THE FLOW OF LYMPH IN NERVES. L. B. ALFORD and S. I. SCHWAB, J. Nerv. & Ment. Dis., **47**:118 (February), 1918.

The hypothesis that there is a flow of lymph in nerve trunks in a central direction has been used to explain the location of the lesion in the nerve roots in tabes, herpes zoster and some other affections, and also to explain some of the phenomena seen in rabies, tetanus and poliomyelitis. This hypothesis has received some experimental confirmation by Orr and Rows, Pironne, Laitiner and others. In attempting to confirm these results, the authors injected a solution of certain iron salts, and of fuchsin, India ink, turpentine and ether into the nerve trunks of animals but found no evidence of the existence of an ascending lymph stream. It was found, however, that when certain substances, particularly turpentine and ether, were injected into nerve trunks, they flowed along under the sheath for long distances and entered the subarachnoid and subdural spaces. This fact and not the presence of an ascending lymph stream may account for the results of other observers. It was also found that ether injected into the infra-orbital nerve in the cheek passes into and causes a degeneration of the Gasserian ganglion. It is suggested that this method might be used in the treatment of trifacial neuralgia.

It would seem to the reviewer that if lymph channels existed in nerve trunks they might be supposed to be of such a delicate type that the traumatism produced by the injection of any foreign substance, and the consequent inflammatory reaction, would most effectually block these channels and so stop the flow that the experimenters were endeavoring to determine.

CAMP, Ann Arbor, Mich.

CLINICAL STUDY OF THE ORIGIN, DEVELOPMENT AND DISAPPEARANCE OF A SYSTEM OF DELUSIONS. L. E. EMERSON, M.D., J. Abnorm. Psychol. **13**: pp. 23-32.

The case is a woman (age is not given) who presents marked delusions of reference (ministers preach at her, sermons published about her, people look at her, talk about her among themselves). This because she is regarded

as immoral on account of her obsession to look at the genital region of men. She was quite depressed about the situation and was anxious to convince her friends that she was not bad but only troubled by a habit she could not control. Emerson gives the following analysis: The patient was a woman of powerful passion ("when I want anything I want it so terribly that I am afraid"). In this respect she is like her mother, but in order to be totally different from the latter she repressed her instinctive feelings. She hated her mother. This as well as the fear of her own desires, Emerson thinks, made her dislike to be a woman. She therefore began to act like a man and wanted to dominate every situation. The patient once dreamed that she was a man. As a result of this struggle she became nervous and the obsession commenced. At this point she wanted advice, but would not go to a man for fear he would take advantage of her and went to a woman for advice. She fell in love with this woman, and the latter becoming frightened repelled the patient. She was now thrown on her own resources and developed the delusions. Emerson says that her libido was now blocked in every way, that she had no outlet in any intellectual life to which she felt she could rise, could not love a woman, nor could she love a man (because it was dangerous). Moreover, she did not want to love a man but to *be* a man. Emerson says her love instinct or her desire to receive and give affection then "degenerated into the obsession of looking and then into delusions."

She began to recover when she became willing to talk and to understand the situation. But the cure came chiefly when she fully appreciated how intense and at the same time how much repressed her desire to be a man really was.

To the reviewer the case illustrates again the fact that an analysis to be therapeutically helpful need not be very thorough but that it merely has to formulate the situation for the patient in such a manner that it can be dealt with, no matter how comprehensive or one-sided this formulation may be. This of course is also the reason why a therapeutic result of an analysis by no means shows that the formulation was entirely correct. The therapeutic accessibility in this case may also depend on the fact that there was considerable depressive affect and that the delusional development was merely superimposed on an obsession and was even in consciousness not entirely cut off from this source.

HOCH, Santa Barbara, Calif.

Society Transactions

PHILADELPHIA NEUROLOGICAL SOCIETY

Regular Meeting, Dec. 18, 1918

MAX BOCHROCH, M.D., *President*

A CASE OF SYPHILIS HEREDITARIA TARDA, WITH "TIP-TOE" GAIT. DR. N. S. YAWGER.

The patient, who is from the service of Dr. Lloyd at the Philadelphia Hospital, is a girl, aged 10 years. The case is of some interest by reason of the tardy development of transmitted syphilis, but more particularly because it shows a very remarkable gait.

Present Trouble.—At 6 years this child began school and two weeks later she said her feet felt as though pins and needles were sticking in them; these pains kept up for a month and then she began to walk on her toes. Her behavior at this time was like that of other children—she talked, played, sang and recited pieces. At 8 years her speech became affected, she showed some disturbance of vision and was becoming noticeably deficient mentally. About six years ago, she developed epileptoid attacks; these occur once or twice in twenty-four hours and last from one to three minutes. In behavior she is irritable, bad-tempered and cannot be easily disciplined; if crossed, she gets into a tantrum—screams, kicks, bites and beats her head and body.

Previous History.—She was born at term and her infancy and early childhood was uneventful. She had a good start and apparently was a healthy child.

Family History.—The father is a laborer of about average intelligence and nonalcoholic. He admits a previous gonococcus infection but denies syphilis. The Wassermann test in the blood is negative. The mother died a few years ago—cause unknown. There had been but one pregnancy.

Examination.—Mentally, this girl is an imbecile; she is emotional, demonstrative and affectionate.

Station.—When standing her feet are rather widely apart and rest squarely on the floor; there is a backward bending of both knees, particularly the left.

Gait.—The child walks as though her extremities were rigid and usually, though not invariably, walks on her toes; she can keep up this gait for a considerable time and even run; the "tip-toe" gait is not due to talipes equinus; it is not constant, and she is not spastic.

Eyes.—There is no nystagmus nor ocular palsies. There is evidence of previous ulcers in the scars on the corneas. The pupils do not respond to light nor in accommodation.

Upper Extremities.—Judging from her volitional movements, they do not seem ataxic. The muscular power is good and the biceps and triceps jerks are equally and bilaterally exaggerated.

Lower Extremities.—These appear almost overdeveloped, both being unusually strong. At times, there is a bilateral patellar clonus; the patellar and

Achilles jerks are markedly exaggerated but there is no spasticity. There is an absence of ankle clonus and Babinski's sign. The sphincters are intact.

Sensory Changes.—Apparently there are none. She has typical Hutchinson's teeth and scaphoid scapulae. The Wassermann test in the blood was negative; two attempts at lumbar puncture gave no fluid.

Roentgenograms.—These were made from the lumbar spine and the knees; all were negative.

DISCUSSION

Dr. J. Hendrie Lloyd said that this child had been observed by him in the Philadelphia Hospital. Dr. Yawger had already called attention to all the features of the case. She has Hutchinson teeth very marked, and she has a rather characteristic history of the development of nervous trouble after she was born. She seems to have been a healthy child in early infancy and to have developed physical and mental deficiencies later on. That was in line with the history of hereditary syphilis as Hutchinson called attention to it many years ago. That is to say, the child may be born apparently perfectly well, and with the exception of some sniffles and some sores about the corners of the mouth and a transient keratitis, it may be practically a well child until 6, 7 or 8 years of age, when it begins to develop serious nervous disorders, such as epilepsy, paralysis and idiocy. This child has developed the ordinary appearance of the disease. The affection of her lower limbs, however, is peculiar. Her limbs are not spastic. She is fairly limber in her legs, but when she begins to run, up she goes on her toes as though by some spastic contraction of the muscles. She has quite typical Hutchinson teeth; also retarded mental development. The fact that the father has a negative Wassermann reaction and that the child has a negative Wassermann reaction has little or no significance. Dr. Lloyd believed in hereditary syphilis; it was commonly found that the child did not have a positive Wassermann in the blood or spinal fluid. This case raised the question as to what we mean by hereditary syphilis. According to the present-day biologists nothing can be hereditary which is not transmitted through the germ plasm. No acquired deficiency or deformity can be transmitted. That being so, and since we discovered that syphilis is a spirochetal disease, the question arises: Is there such a thing as hereditary syphilis? Biologists tell us that the spirochete is larger than the spermatozoon, it is larger than the ovum. If that is so, how can the spirochete get inside the spermatozoon? How can a spirochete be transmitted through the germ plasma? Hutchinson wrote of syphilis with remarkable prevision thirty years ago. He knew nothing about syphilis being due to a micro-organism, but he believed it was. He referred to the fact that some writers refuse to believe that hereditary syphilis can be transmitted from the father because of this very difficulty of seeing how the micro-organism could be transmitted through the spermatozoon. If that is true, hereditary syphilis is a misnomer. What we have in these children is acquired syphilis—acquired in embryo through the mother. In other words, it is congenital syphilis. Dr. Lloyd thought this child showed clinically fairly good evidence that she presents a case of retarded congenital syphilis.

Dr. Charles W. Burr said that he had seen quite a few imbecile children who had very curious gaits that were not due to an organic disease, but were mental. They were habits that the child had acquired, and he rather doubted whether in Dr. Yawger's case the gait had an organic basis. Of course, the child was an imbecile and a syphilitic and all that, but Dr. Burr

was not convinced that it was due to a gross disease in the cerebral cortex. He would be inclined to believe, until the postmortem comes, that this was a trick in walking that the child had acquired. Imbeciles are very prone to all sorts of tricks, grimaces, dancing, etc. Dr. Burr thought it was quite possible that this condition instead of being a physical thing—he said he was speaking now of the gait rather than of other symptoms—that the gait may be mental rather than due to gross organic disease.

Dr. Augustus A. Eshner said he wondered whether one had not a right to ask for better evidence as to the syphilitic nature of this case? He thought that so-called Hutchinson teeth were not an infallible evidence. They were observed in association with other nutritional disorders, as has been shown. In the absence of the Wassermann reaction in the child and in the father, it seemed to be taking a liberty to describe this as a case of syphilis. The evidence was against syphilis rather than in favor of it.

Dr. Alfred Gordon said that the manner with which she stepped on her toes in order to walk reminded him of cases of extracapsular lesions. It resembled in one respect a case which he had named extrapyramidal hemiplegia and which he had exhibited before the Society. The moment the man attempted to move his hand, immediately there would be marked rigidity and spastic contraction of the extensor muscle. If he did not attempt to exercise the muscle the arm remained in exactly the same position as before. The moment an attempt was made to touch him or make active and passive movements, immediately the arm became rigid. When the child attempts to walk the flexor muscles of the legs become rigid. Here is a child mentally abnormal, which suggests some malformation of the central nervous system. The question in Dr. Gordon's mind was whether the extrapyramidal area was constitutionally abnormal so that stimulation of it produces rigidity of muscles controlled by that area. In regard to Dr. Lloyd's remark about hereditary syphilis, Dr. Gordon asked him to recall some facts reported in the literature in which some very young children supposed to have hereditary syphilis, had their spinal fluid and blood inoculated into animals, and spirochetes were found in the testicles. Dr. Gordon said he would then believe that even in the absence of the possibility of finding directly spirochetes in children they may be syphilitic through heredity.

Dr. Nathan P. Stauffer said that if a nose and throat specialist might be permitted to ask a question, he had been wondering whether this child might have this trouble from infantile paralysis. The reason he asked was this: He had under his care some boys and at the time of the epidemic one of them died from the respiratory type of infantile paralysis and a number of boys who were in contact with that boy, and whom Dr. Stauffer was positive did not have disease of the vocal chords before, have since shown paralysis of the vocal chords. He wondered that in a number of the cases we see in which we are in doubt as to what causes the condition if the cases may not be due to infantile anterior poliomyelitis.

Dr. G. Lane Taneyhill remarked that apropos of a negative Wassermann in the blood serum in this patient (the mother not having been examined), this fall he saw a boy, aged 15 years, who is the physical size of a boy of about 11 years, and who had an undoubted case of tabes dorsalis. One of two undoubted juvenile cases of tabes Dr. Taneyhill has seen. The Wassermann was negative in the blood serum both before and after eight injections of arsphenamin, but the spinal fluid was positive—with 33-cells positive Wassermann reaction—and the colloidal gold reaction gave the paretic curve.

Both father and mother were examined; they revealed no signs of nervous disease and they cooperated far enough to have a Wassermann test made, but it was negative in both of them; but the spinal fluid of neither the father or mother had been examined. He thought it was very desirable to have the spinal fluid obtained from this child. That the blood Wassermann was negative did not exclude nervous system syphilis.

Dr. N. S. Yawger in closing the discussion, said in regard to the condition having resulted from infantile paralysis — unquestionably, the cerebral form could give rise to some of these symptoms; but here, the onset was slow and the child had many symptoms common to congenital syphilis including Hutchinson teeth, scaphoid scapulae and scars on the cornea. As to such teeth, these are typical of what Hutchinson described. It has already been remarked that a negative Wassermann is by no means uncommon in congenital cases. The comments by Dr. Burr on the gait, conform more nearly to what Dr. Yawger had in mind. Dr. Yawger had already remarked that the lower extremities were strong—appearing almost overdeveloped. Despite negative roentgenograms of the knees, there was an obvious defect at those joints, and he was inclined to believe that the gait was largely one assumed by the child to overcome the weakness at the knees.

A CASE OF MEDIAN NERVE INJURY, DUE TO STAB-WOUND FROM ULNAR SIDE OF HAND. Presented by Dr. T. E. Shea (by invitation).

Summary of Case.—The case presented is peculiar from the fact that a stab-wound in the hypothenar or ulnar side missed the ulnar nerve and injured the median. After a process of anatomic deductions, the injury was located in the median nerve at its emergence from under the anterior carpal ligament. Physiologically considered the deduction was made that the superficial fibers were injured, as it involved mainly the sensory distribution. Trophic disturbances were present which lead to thoughts, concerning the great factor displayed by normal nerve force in infections. The trophic disturbances in this case were compared to the limited gangrene of diabetes mellitus, and the belief expressed that ordinarily infection could not progress unless toxins destroyed the nerves controlling the protective forces of tissue.

DISCUSSION

Dr. J. Hendrie Lloyd said that trophic lesions following injuries to the median nerve had been reported. A case was reported some years ago by Haldor Sneve in which injury to the median nerve was followed by painless whitlows on the ends of the index and middle fingers resulting in loss of the distal phalanx in each of these fingers. Dr. Lloyd thought that was one of the risks in this case. Motion is not so much impaired in injuries to this nerve as might be expected.

Dr. Charles S. Potts said that he was considerably interested in the trophic disturbance in this boy's fingers because he had seen two cases of injury to the median nerve in which there was great liability to trophic ulceration in the skin area supplied by this nerve. In one of these cases a blister appeared on the end of the thumb. It finally dried up and left an area of sluggish ulceration which was very slow in healing and only did so as the other symptoms improved. The nerve was not divided, but injured.

Dr. Potts inquired if injuries to the median nerve were more likely to cause trophic disturbance of this sort than injuries to other nerves. Dr. Potts had also seen a woman the other day in whom an injury to the median nerve had caused symptoms similar to those of this man, and she had a little blister on one finger which looked as though it would break down and ulcerate.

Dr. Francis X. Dercum said that one thing that would account for the freedom of escape of the ulnar nerve was the fact that it lies more superficially than the median. The knife entered well into the body of the hypothenar eminences and in that way the ulnar nerve lying practically above this level it escaped. The interference with the ulnar was very slight, if indeed any. Dr. Dercum asked the patient how much pain he noticed when it happened, and the patient replied, "No pain at all. My whole hand was numb."

Dr. T. E. Shea, in closing the discussion, said that in speaking of this case he had drawn the differentiation between the sensory and the motor fibers. Some authorities, which at the present time he could not quote, claimed that the superficial fibers of the nerve trunk were purely sensory fibers, while those which lie deeper were the motor fibers. If that particular fact held true the cut must necessarily have simply affected the superficial fibers of the nerve trunk. Speaking of the trophic disturbances, he mentioned the fact and asked what part the nerve force played and whether the trophic disturbance in this particular nerve involvement was not something like the diabetic gangrene we see.

HYSTERIA WITH MULTIPLE OPERATIONS. Presented by Dr. Francis X. Dercum.

Previous History.—The patient was a woman, aged 27, from the wards of the Jefferson Hospital, and gave a history of five major operations for the relief of pain, none of which had been successful. The patient was unmarried; housemaid by occupation. No facts of importance were elicited in the family history. She had suffered from the ordinary diseases of childhood, had begun menstruating at the usual time, but at 17 had been nervous and had frequently suffered from convulsive seizures. At this time (1908) an appendectomy was performed. Subsequently (1910), a laparotomy for the removal of an ovary; in 1912, a gallbladder operation was performed. In 1915, an operation was performed for nephropexy, and in 1917 this operation was repeated.

Present Symptoms.—The patient presented no evidences whatever of any organic nervous disease nor of any visceral disease. While at the hospital, she had suffered repeatedly from hysterical convulsions and had complained of severe pain in the right side of the abdomen. At times, this was referred to the groin, to the right side of the abdomen. At times to the right lumbar region.

Examination.—This revealed marked areas of cutaneous painful hyperesthesia, but no tenderness or pain could be elicited on deep pressure. While Dr. Dercum could not, of course, claim that the operations performed had not been necessary, the patient herself stated that the symptoms from which she suffered had not been in any way relieved. It is more than probable that the pains of which she had complained and which had stimulated possible visceral disease had been purely hysterical in nature.

DISCUSSION

Dr. Charles W. Burr said he thought it was a very common thing for hysterics to be operated on. Indeed, he sometimes thought that there were some surgeons who had no conscience at all. Also, in organic disease Dr.

Burr said he fancied that every man present had had at least one case of locomotor ataxia which had been operated on. At the Orthopedic Hospital about every eighteen months a patient comes to show a scar of an operation which was done in perfect good faith.

Dr. Sherman F. Gilpin said that he had recently seen a patient who had been frightened in school at 14 and lost her voice. Since then she had had seven abdominal and two nose and throat operations in twelve years.

Dr. Alfred Gordon said this question of useless operations was very common. It was so ordinary that you look for it and as far as the conscience of the surgeon was concerned he would rather say that it was not their fault mostly. The patient is directed by the general practitioner to the surgeon with request for operation. The patient complains of pain in the abdomen. They find anteversion and all sorts of abnormal conditions of the uterus and refer all nervous trouble to that, to movable kidneys, to gastroptosis and accordingly the patient is operated on; after the operation he is just the same as before. Dr. Gordon remembered one case several years ago which impressed him so much that he could never forget it: A young man of splendid appearance, who made the rounds of the hospitals for pain in the abdomen was treated in many ways. All sorts of diagnoses were made—dilatation of the stomach, and many others. He was massaged, even sounds were passed, cystoscopy was performed, and one surgeon advised the removal of part of the colon. Finally, he developed pain in the right side of the hypochondrium and was referred to a prominent surgeon who advised an immediate operation. Later in the evening the patient was put on the table; the patient being very emotional and excitable, saw the surroundings, physicians with white aprons and coats and instruments around. He became frightened, and jumped off the table and ran away. From that time he never had a pain.

Dr. Francis X. Dercum said that he felt that his experience was not unique in this particular matter because there must be frequently recurring cases with multiple scars. Still, we must be very careful in regard to what we do and say. Dr. Dercum remembered many years ago when Dr. Osler sent him a patient who had an interesting case of abdominal pain. The man had pain in the epigastrium. He had been studied at the Johns Hopkins Hospital without any very definite result. He had acquired the morphia habit because of the pain, and when the man was sent to Dr. Dercum he withdrew all morphia, and then the patient became more than doubtful as to whether he had not a real organic basis for his pain. Dr. Keen operated and a small ulcer was found over the wall of the stomach. That man had an actual cause for his pain. That was not a case of hysteria. The diagnosis lay between tabes with gastric crises or gastric ulcer. Dr. Dercum finally persuaded him to have an exploratory operation performed. Dr. Dercum said he did not believe in exploratory operations as a rule. He thought this frequency of exploratory operations in nervous cases was a very serious matter.

TWO CASES OF FRIEDREICH'S ATAXIA APPEARING VERY EARLY IN LIFE. Presented by Dr. Francis X. Dercum.

Dr. Dercum also exhibited two boys—brothers— aged 6 years and 4 years, respectively, both presenting the symptoms of a typical Friedreich's ataxia. The patients had been referred to Dr. Dercum's wards of the Jefferson Hospital by a nearby charitable institution.

Previous History.—The family history that could be elicited was rather scanty. However, it was learned that the father is living and is about 35 years of age; that he was unable to walk alone until about 9 years of age; that he comes from a strongly alcoholic family and is himself an alcoholic. Even when sober, he is said to walk as though intoxicated.

Present History.—The personal history of the older child is as follows: He has been apparently in good health aside from his present affliction. The patient had been abandoned by his parents in the early months of life and has been cared for in a public institution. He has only begun to walk during the past eighteen months. His gait is markedly ataxic; stands with his legs widely separated, and sways as though about to fall. The knee jerks are lost; there is a faint Babinski reflex on the left side, but no other feature of moment. The younger patient, aged 4, presents symptoms very much like those of his brother and equally pronounced; loss of knee-jerks, but no Babinski sign. Both of these cases are of interest because of the unusually early age at which the symptoms have made their appearance.

A CASE OF TABES DORSALIS SHOWING RESULTS OF TREATMENT, INCLUDING DRAINAGE OF CEREBROSPINAL FLUID.

Presented by DR. SHERMAN F. GILPIN.

This was a case of tabes dorsalis, showing effects of treatment by inunctions of mercury, with drainage of the cerebrospinal fluid.

History.—The patient, Mrs. A. K., a white woman, aged 49, was admitted to the Jefferson Hospital clinic in June, 1917. She is the mother of six living children and all of them in good health. Her present illness began four years ago with pain in left leg. Shooting pains in arms, neck and face have been marked.

Examination.—Physical examination shows typical Argyll Robertson pupils, diminished knee-jerks, and ataxia of gait and station. The ataxia was well marked and the patient so ill and weak it was necessary that some one accompany her on her visits to the clinic.

Laboratory tests on admission showed: Blood Wassermann, +; fluid Wassermann, ++++; lymphocytes, 48. Laboratory tests in March, 1918, showed: Fluid Wassermann, ++; lymphocytes, 43. During the last three months several Wassermann tests of the spinal fluid have been negative and no lymphocytes were found except at the last examination when the report is 4 cells per cubic millimeter.

Present Condition.—At present the patient feels well, has gained weight, stands well with the eyes closed and can walk the streets as well as she ever could. She has used mercury by inunction faithfully to the physiologic limit. Her spinal fluid has been drained thirty times.

DISCUSSION

DR. FRANCIS X. DERCUM said that it seemed at first sight difficult to account for the benefit of drainage in tabes and paresis. It occurred to Dr. Dercum that the explanation was as follows: If the pressure in the dural sac is increased, it must mean that less blood can flow into the cord than normally. If the pressure be suddenly reduced, a passive hyperemia of the cord probably ensues. You have here a method which is comparable to the Bier method in surgery. In the second place, if the spinal fluid is drained thoroughly, toxic

bodies must also be removed. Dr. Dercum said they took away 50 or 60 c.c. with great benefit. He was quite sure some of these patients would get much better even without the inunctions, just from drainage itself.

Dr. Gilpin, in closing the discussion, said that Dr. Dercum had answered a question by Dr. Burr. He drained all the fluid that would run out. A week or two ago he took the fluid from a case of tabes for another physician and in a couple of days he reported to Dr. Gilpin that the patient was deaf. Dr. Gilpin saw her the next day. He could not make her understand by yelling in her ear. In three days she had recovered. Another thing—in taking fluid from a tabetic there is no following headache, whereas in the nonsyphilitic the patient has severe headache following spinal fluid withdrawal.

NYSTAGMUS ON MONOCULAR VISION. Presented by Dr. Alfred Gordon.

History and Examination.—A girl, aged 16, commenced to complain of poor vision six years ago. She improved under some treatment. Several months ago there was a return of the condition. When she came under the author's observation, the following symptoms were noticed: On monocular vision nothing abnormal was present. When one eye was covered the other eye immediately assumed the state of lateral nystagmus with the quick movement externally. Moreover, when the patient having both eyes uncovered would turn them externally to the extreme angle, either eye could not remain fixed in the external angle but would tend to move away. The pupils and eye-grounds were all normal. The patient also presented some atasia of the left hand in the pointing test and diminished knee-jerk on the left side.

Treatment.—Although the Wassermann reaction of the blood was negative, nevertheless, she was placed on mercury and iodids. There was considerable improvement in the power of the external recti muscles to hold on when the eyes were placed in the extreme external position, the atasia of the hand disappeared totally. The nystagmus on monocular vision remained unaltered.

Comment.—The condition of the eye-globes—namely, the nystagmus and the inability of the external recti to remain in a fixed position—point either to a congenital weakness of the latter muscles or to a lesion in the muscles of both sixth nerves.

DISCUSSION

Dr. Francis X. Dercum said that the little girl looked to him as though she had rather prominent eyes, rather a large thyroid, and rather a rapid pulse. Have we not, perhaps, here a case of hyperthyroidism or exophthalmic goiter associated with the nystagmic involvement?

Dr. William G. Spiller said that in examining the patient he had observed a phenomenon which Dr. Gordon had not mentioned. Dr. Gordon had stated that the external recti muscles were weak, but Dr. Spiller had noticed that this weakness like the nystagmus was distinct only in monocular vision. When the girl looked to the right or left with both eyes opened the weakness of the external recti muscles was not evident, but if she closed one eye the outward movement of the other eye was very imperfect and the eyeball could not be held well in the outer canthus. It was evident that the innervation of each external rectus muscle in binocular vision was greater than in monocular vision, and probably the innervation of the internal rectus muscle of one eye

caused an overflow of innervation to the external rectus muscle of the opposite eye. While this double innervation might occur to some extent with one eye closed, it was greater with both eyes open, and was then sufficient to overcome the slight weakness of the external rectus muscle, which possibly was congenital.

The nystagmus occurred under precisely the same conditions, and it was reasonable to associate one phenomenon with the other. The nystagmus occurred only in monocular vision probably because of the weakness of the external rectus, which being slight did not prevent the eyeball from moving outward, but was sufficient to prevent it from being held firmly; and in the attempt to fix the eyeball repeated innervation was necessary and a pseudo-nystagmus was thus produced. A pseudo-nystagmus may readily be observed in a person looking out of the window of a rapidly moving train, as the eyes are rapidly losing from vision the object fixed and a new object is equally rapidly coming into the visual field.

Dr. G. Lane Taneyhill said that he would suggest that the weakness of the external rectus was not sufficient to give the patient a squint. It was weak only enough to cause a little swinging inward on monocular vision which she tried immediately to correct, producing "nystagmus." This suggestion accepts Dr. Spiller's observation.

Dr. Dercum said that nystagmus was a positive sign. It was not a sign of mere muscle weakness. A muscle may, at times, present a nystagmoid movement which comes to rest after a while, but is a positive symptom.

Book Reviews

THE PSYCHONEUROSIS OF THE WAR. By Dr. G. Roussy, Assistant Professor in the Faculty of Medicine, Paris, and J. Lhermitte, sometime Laboratory Director in the Faculty of Medicine, Paris.

Translated by Wilfred B. Christopherson: Edited with a prefatory note by William Aldren Turner, C.B., M.D., Temporary Colonel, Army Medical Service and Consulting Neurologist to the Forces in England. Published by the University of London Press, Ltd., in the Military Medical Manuals.

To the neurologist, especially one who has taken up military duties, this will prove one of the most interesting books resulting from the war. The psychologist will perhaps be disappointed that the authors do not go more deeply into the mental mechanisms involved in the production of these conditions, although no one will doubt for a moment their practical understanding of the underlying mechanisms when the results of their treatment are considered.

One of the fundamental elements in the causation of the psychoneuroses is certainly emotional shock but this alone does not suffice to produce the symptoms. In the normal individual, emotional phenomena, however violent they may be, are restrained by force of will by personal self-control; then, when the emotional cause has ceased to act, they fall into oblivion, effaced by the perceptions, the preoccupations and the associations of daily life.

In the neuropathic subject the war brings an almost continual recrudescence of these emotions, which added to bodily fatigue, begets in one already predisposed "a highly emotional condition and emotional receptivity."

The initial emotional condition is not necessarily followed immediately by psycho-neuropathic symptoms; a latent period — a period of incubation — is interposed between the causal emotion and the onset of these symptoms. The soldier profoundly impressed by the conditions and often experiencing the most distressing visceral disturbances from the emotion, reacts, driven by that instinct deeply rooted in us all—that of self-preservation. Shaken by a bursting shell, for example, he has nevertheless the energy to escape from danger. Far from being glued to the spot, he shelters in a dugout, a shell hole or a trench. It is when removed to calmer surroundings, far away from danger, that the psycho-neuropathic condition comes to light, whether as a contracture, a paralysis, a tremor, or a convulsive fit.

Exception might be taken to the authors' statement that "this is easily understood if we bear in mind that from the moment when all danger is passed, the instinct of self-preservation loses all its inhibiting influence over the emotional phenomena," and "we thus reach the third act of the series, the fixation and realization of the emotional reaction." One would say rather the emotion is the natural reaction to the stimulation of the instinct of self-preservation, and it is the will-power alone influenced, it is true, by the instinct which exerts the inhibitory restraint over the emotional reaction. The individual having reached a place of comparatve safety has a free opportunity to react fully to the emotion; during which emotional reaction the action of the higher intellectual processes which normally govern the will-power and self-control are disturbed or altogether in abeyance, and the desires incited by

the instinct of self-preservation hold sway. During the period of inactivity of the higher intellectual processes any auto-suggestion or hetero-suggestion which agrees with the desire present is accepted, and so we reach the development of the psychoneuropathic manifestation, be it a contracture, a paralysis, a tremor or a convulsive fit, mutism or delirium. It is not the "restraining bridle rein of self-preservation" being no longer present which allows this fixation and realization of the emotional reaction, but it is precisely the desires set up by that same instinct of self-preservation in the absence of the activity of the intellectual censor which incite this psychoneuropathic manifestation; otherwise, why do we not see similar manifestations in German prisoners, and why do the Germans remark on the absence of these same manifestations in our men whom they have captured? Surely in them the restraining bridle rein of the instinct would be removed, or at least very considerably loosened.

This is by no means a distinction without a difference, because, if my view be correct, it immediately puts into our hands a reasonable and practical method and guide for treatment; whereas if the authors' interpretation is right then it is impossible to explain the rationale of their method of treatment except by inferring that they by their electrical applications excite the instinct of self-preservation to such an extent that it again puts on the restraining inhibiting influence. This I do not believe.

My interpretation of the successful results reported by the authors is that the patient is put in such a position that his desires are guided into proper channels and an incentive is given him to have the will to control his neuro-psychopathic disability.

The authors lay stress on the fact that the faradization must be continued until the patient is "mastered," which, as I have analyzed it, means until a negative self-feeling is inspired in him which will render him more suggestible and more amenable to reason.

The book increases in interest as we proceed: detailed description is given of all the varied characteristic forms of neuro-psychopathic disability, and one is struck with the similarity of the experiences of those in the French army to what neurologists in other armies have described. The writer has seen instances of every type the authors describe but cannot add any types that they have omitted.

The chapter on the predisposing and exciting causes leaves little to be added. The exact method of treatment will vary according to the personality of the physician. The chapter on this subject should be of great assistance, and should be followed with an intelligent appreciation of the object aimed at.

I think one will find that as he gains in experience and, what is perhaps more important, creates an atmosphere of optimism, faith and cure, he will resort less and less to the use of the faradic current and depend to a greater extent on the other parts of the methods outlined—namely, the preliminary careful general examination, then the sincere sympathetic explanation of the true cause of the development of the symptoms followed by verbal persuasion to complete cure. Isolation during this period is certainly a useful adjunct to the treatment.

The appreciation of the fact that the physical disability is merely an outward evidence of the underlying mental disturbance renders a more or less prolonged course of physical and psychical reeducation with occupational therapy necessary. "The cure of a psycho-neuropath really consists of a mental contest, resulting in the victory of the physician. This, in conclusion, is the secret of psychotherapy."

The final chapter is devoted to the military decisions affecting the disposal and pensionibility in these patients. These decisions were inspired by the Neurological Society of Paris and will justify the serious consideration of the military medical authorities of the Allied Armies. I may say they have been adopted in the Canadian Army and are proving eminently successful. The rationale of these decisions I think will be found to conform to the interpretation which I have attempted to advocate in the above lines.

COMMOTIONS ET ÉMOTIONS DE GUERRE. Par ANDRÉ LÉRI. Paris, 1918.

This booklet is one of the well known series of French medical war manuals, "Collection Horizon," published by Masson et Cie.

Much of what has been written on the subject of "shell shock" has been based on incomplete experience. This is true not only of publications which appeared early in the course of the war, but also of later publications, the latter having been produced for the most part by medical officers working not in the zone of the advance but in neuropsychiatric centers where they could see only cases evacuated to the rear, and these but in the later stage of their course. These cases constitute a small proportion, and are not representative of the total.

The same is not to be said of the work under review. The author had witnessed war neuroses at the front, in field hospitals, and in neuropsychiatric centers in the interior, and presents a summary of his observations in the light not only of his own four years' experience, but also of the views of other observers.

The principal message of the book seems to be to point out the heterogeneity of "shell shock" and particularly to draw the distinction between true concussion and purely emotional disorders. Among other subjects treated are cerebral contusion, focal traumatic lesions, war psychoses, and hysterical disorders.

In an introductory chapter the questions are raised: Can one, on the battlefield, in the first aid station, in the field hospital, or in the base hospital, distinguish a case of concussion from one of emotional disorder? Of what importance is it to make that distinction? The answers given are: At the front, cases of concussion and of emotional disorders behave differently; the first effects having passed, the symptoms are still distinguishable on the patients' evacuation to the rear, and even later the sequelae following the two conditions are often different in aspect and course; these differences should be recognized, as the treatment of the two conditions is as dissimilar as their general course and their immediate and ultimate prognosis.

Cases of concussion vary in their clinical aspect. Five general types are described as follows:

1. A large shell bursts overhead or a bomb drops in a trench and explodes at a distance of a few meters from a soldier. He is thrown violently, unconscious. He may die without a movement or a cry, though not touched by a fragment. This may be termed *fulminating concussion.*

2. If death without wound is relatively rare, *immediate loss of consciousness* is, on the contrary, the rule. The soldier falls where he may happen to be, perhaps in full exposure to barrage; there he remains regardless of danger. He is taken up and carried to the first aid station either on a litter or by his arms and legs. He is inert, arms and legs hanging or swinging, body sunken, head hanging, chin on chest. On examination, he is completely unconscious, limp, his face pale or, more often, cyanotic; often he bleeds from the nose or

ears. If the examiner raises a limb and then lets go, it falls heavily like a dead weight; if pricked or pinched the soldier does not stir. He responds to no question. All tendon reflexes are abolished or greatly diminished; *the pupils are widely dilated* and react but very slightly to light; *the pulse is slow* and weak; respiration is slow and stertorous. The patient is often soiled with urine or fecal matter—sometimes with vomited matter.

3. In other cases, the patient, instead of being an inert mass, presents a certain rigidity; the limbs are not limp, the head does not hang. When an arm or leg is raised it does not fall back so heavily; if the patient is pricked or pinched he will groan and withdraw the limb; if spoken to in a loud voice or if shaken by the shoulder, he will answer, always slowly, painfully, in monotonous fashion in monosyllables, in stereotyped words, but nevertheless distinctly and correctly without confusion. Thus one patient responded to all questions with the words *head, shell, cold;* but these words were not used at random, but with perfect relevancy to the questions put to him. The limbs may be animated by semiconvulsive trembling. All tendon reflexes are increased, sometimes unequally on the two sides.

4. In still other cases the patient likewise falls where he may be, a complete stranger to the instinct of self-preservation. Often he, too, is lifted by stretcher bearers, but he can to some extent support himself, and he is brought to the first aid station by being supported under the arms. If released on the way he tends to fall again. Every movement is extremely painful and the feet seem to drag a weight at each step. At the first aid station he, too, lies inertly where he may be left; but he groans, complains if made to move, answers questions, complains of headache. However, he does not know where he is, nor why he is there, nor what has happened to him, and, when the questioning is discontinued, falls back into his inert, clouded state, indifferent to his surroundings. Here, too, the pupils are generally dilated and the pulse slow.

5. Finally, in a small group of cases, the soldier, more or less stunned by the shock of a violent explosion, but not thrown, presents signs of lesions in the nervous centers—organic paralyses, aphasia, jacksonian convulsions, blood in the spinal fluid—but *no loss of consciousness.*

An interesting group of cases occurred under the following circumstances. A 90 mm. gun was partly concealed in a hole about 1 meter in depth and about 4 meters square. To the left, in a small dugout four artillerymen were seated in a row. A large shell fell to the right of the gun, exploded, and turned the gun over on its left side. Of the four men, the two nearest the opening of the dugout were found dead, still seated, with faces swollen and livid, blood running out of their nostrils and ears; they had no wounds. The third was drowsy, immobile, but was breathing well and answered questions in monosyllables; he was wounded in the arm; he was brought out, his wound dressed, and he was evacuated to the rear. The fourth was in the farthest end of the dugout; he, too, was brought out; in the fresh air he seemed inert for a few seconds; then while his comrade's wound was being dressed, he suddenly stood up and ran away as fast as his legs could carry him. Thus, side by side, according to the distance from the point of the explosion, in a dugout but 1½ meters in depth, there was death from concussion and the clinical pictures of concussion and emotional disorder.

The emotional disorders are in striking contrast with concussion. Whether in more or less close proximity to a large shell, bomb, or mine explosion, or at a good distance from a projectile of large or even small caliber; whether he had witnessed, even from afar, some terrifying scene in which explosives

have played no part; whether thrown or not; in any case, *the patient has not lost consciousness.* If thrown, he quickly gets up again; if going forward, he turns back, and that quickly, if possible at a run, or else limping or staggering, and arrives *alone* at the first aid station. With haggard look, pinched nose, pale face, wild expression, he throws himself into the farthest corner of the first aid station, sits down on the ground or on a bench, all huddled up, and does not budge.

An attempt at examination finds him incooperative, trembling, rigid; respiration panting, *pulse rapid* and strong, pupils *rather small;* but the tendon reflexes are neither increased nor diminished, the pupils react well to light, patient is not wet or soiled.

He will not answer questions; seems not to hear, to be mentally absent. This is the same subject who, the next day, in the field hospital, or later, in the base hospital, will say, though in good faith, that he had lost consciousness and can recall nothing. In reality he has not lost consciousness and can recall everything perfectly; one needs but know how to question him; but in the meantime he is *exclusively preoccupied with his anxiety,* indifferent and inattentive to everything save that which concerns the instinct of self-preservation.

In the first aid station the patient will not locate himself at random. He will look over the ceiling and the walls and often quickly change his place for greater security.

When the ambulance comes to evacuate the wounded, these men, who seemed incapable of voluntary activity, rush outside before one has had time to call them and install themselves normally in the twinkling of an eye. If the ambulance cannot come as far as the first aid station, it suffices for the corporal of the litter squads to ask the medical officer what patients should be carried on a litter; they all immediately answer that they can walk; one gets there faster by walking, at the same time better concealing himself than on a litter.

Of the three principal conditions described in the book—contusion, concussion, and emotional disorder—*the last is by far the most commonly seen* in the first aid station; contusion comes next; not more than four or five cases of true concussion are seen for 100 of emotional disorder.

At the field hospital, and from there on, the syndromes often become less pure. The case of concussion or contusion, on recovery of consciousness, cannot but become more or less emotionally affected by the thought of the great danger which he had escaped and of others to which he may yet be exposed. On the other hand, the emotional patient, finding himself henceforth secure, no longer has his physical and mental activity given over to self-preservation; he is often but a mere case of marked fatigue and, as such, by his depression and inhibition, resembles the case of concussion.

Careful investigation still reveals, however, unmistakable contrasts. As the cases of concussion recover from their physical asthenia, with its characteristic mydriasis and slow pulse, and from the mental dulness, they begin to complain of headache and attacks of dizziness in which, for the moment, everything becomes black and silent. The most frequent termination is complete recovery; all confusion of memory soon disappears; but one recollection is forever impossible—*that of the accident itself* and of a period of greater or lesser duration following it.

The emotional patient arrives at the field hospital bewildered, tired, seemingly inert; if spoken to, will not answer. If one disturbs his somnolence by shaking him or shouting in his ear, he moans, stirs, looks up with a terrified expression, eyes widely open, as if possessed by great anxiety or some hor-

rible vision. Later, on becoming more accessible, when questioned about the accident, the almost invariable response is, "I remember nothing"; he will say, however, that he suffered a "concussion," that a shell dropped close by and exploded. He has, in fact, but one recollection which has survived in his memory, *that of the accident itself*. Yet, with this as a starting point, persistent and tactful questioning gradually elicits details of place, time, occurrences preceding and following the accident, until it becomes clear that the patient had at no time lost consciousness. As Léri puts it, *"Ce grand amnésique n'a pas d'amnésie du tout!"*

Only a minority of cases of concussion or emotional disorder reach the base hospitals—a fact which has often been lost sight of, thereby causing much misapprehension and confusion. By the same nomenclature medical officers of the zones of the advance, communications, and supplies have been alluding to different categories of patients. Léri's descriptions of cases in base hospitals ring truer than the descriptions given by observers who have not been put on their guard by such experiences as he has had at the front and in field hospitals. Of special interest is his attitude in relation to hysteria, to which he devotes a brief chapter.

Many writers have shown a tendency to confound emotional with hysterical disorders. But according to Léri it is a mistake to think that hysterical manifestations are an integral and necessary part of the emotional syndrome. They can appear independently of all emotion; and the emotional syndrome has nothing in common with hysteria. A remarkable fact is that hysterical manifestations never appear except when the patient is in a place of security: in a trench, a dugout, in a first aid station. Moreover, they disappear, as by magic, either when security is diminished, as by the dugout being shelled, or when the ambulance is in sight for the evacuation of the wounded. Often they appear during the period of artillery action in preparation for an attack; but never has an hysterical convulsion or paralysis been seen in the open on the battle-field, under exposure to a barrage—"a fact which seems to us of major interest for the understanding of the pathogenesis of hysterical disorders."

Speaking in particular of refractory hysterical phenomena, Léri says, "In all cases they originate not in emotion, but in reflection, when emotion no longer exists; they originate in the idea of retirement on pension with its double benefit of further removal from danger and pecuniary indemnity."

The material so vividly brought to light by the war has its analogies in peacetime neuropsychiatric experiences. The lessons learned in the war so well presented by Léri should be of permanent value.